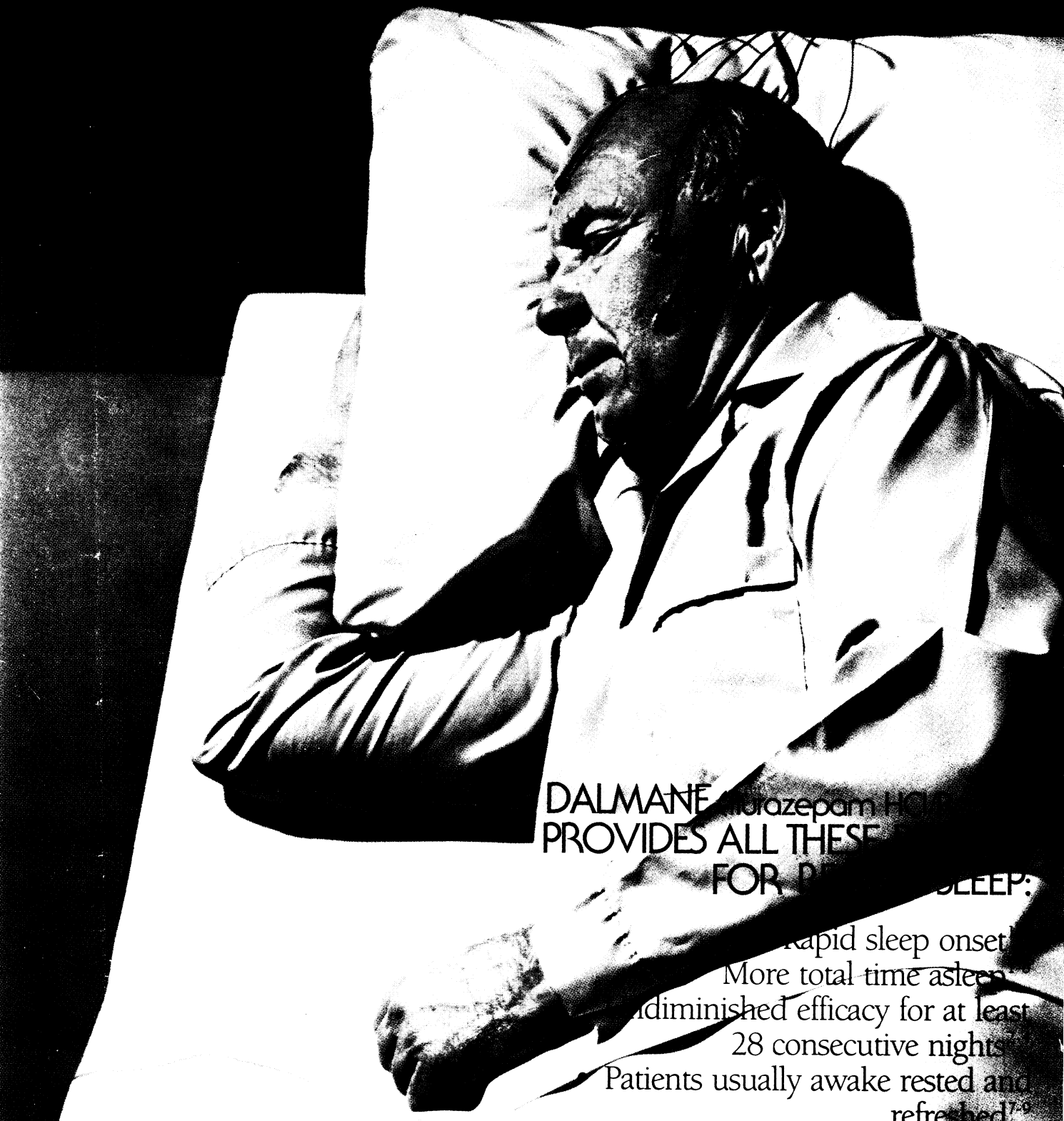
DOCUMENTED IN THE SLEEP LABORATORY[1-5]...



DALMANE flurazepam HCl
PROVIDES ALL THESE
FOR P[illegible]SLEEP:

- Rapid sleep onset[6]
- More total time asleep[6]
- Undiminished efficacy for at least 28 consecutive nights[7]
- Patients usually awake rested and refreshed[7-9]
- Avoids causing early awakenings or rebound insomnia after discontinuation[2,5,10-12]

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DALMANE® Ⓥ
flurazepam HCl/Roche

References: **1.** Kales J *et al*: *Clin Pharmacol Ther 12*:691-697, Jul-Aug 1971. **2.** Kales A *et al*: *Clin Pharmacol Ther 18*:356-363, Sep 1975. **3.** Kales A *et al*: *Clin Pharmacol Ther 19*:576-583, May 1976. **4.** Kales A *et al*: *Clin Pharmacol Ther 32*:781-788, Dec 1982. **5.** Frost JD Jr, DeLucchi MR: *J Am Geriatr Soc 27*:541-546, Dec 1979. **6.** Kales A, Kales JD: *J Clin Pharmacol 3*:140-150, Apr 1983. **7.** Greenblatt DJ, Allen MD, Shader RI: *Clin Pharmacol Ther 21*:355-361, Mar 1977. **8.** Zimmerman AM: *Curr Ther Res 13*:18-22, Jan 1971. **9.** Amrein R *et al*: *Drugs Exp Clin Res 9*(1):85-99, 1983. **10.** Monti JM: *Methods Find Exp Clin Pharmacol 3*:303-326, May 1981. **11.** Greenblatt DJ *et al*: *Sleep 5*(Suppl 1):S18-S27, 1982. **12.** Kales A *et al*: *Pharmacology 26*:121-137, 1983.

DALMANE® Ⓥ
flurazepam HCl/Roche

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening; in patients with recurring insomnia or poor sleeping habits; in acute or chronic medical situations requiring restful sleep. Objective sleep laboratory data have shown effectiveness for at least 28 consecutive nights of administration. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or recommended. Repeated therapy should only be undertaken with appropriate patient evaluation.

Contraindications: Known hypersensitivity to flurazepam HCl; pregnancy. Benzodiazepines may cause fetal damage when administered during pregnancy. Several studies suggest an increased risk of congenital malformations associated with benzodiazepine use during the first trimester. Warn patients of the potential risks to the fetus should the possibility of becoming pregnant exist while receiving flurazepam. Instruct patient to discontinue drug prior to becoming pregnant. Consider the possibility of pregnancy prior to instituting therapy.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. An additive effect may occur if alcohol is consumed the day following use for nighttime sedation. This potential may exist for several days following discontinuation. Caution against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Potential impairment of performance of such activities may occur the day following ingestion. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, abrupt discontinuation should be avoided with gradual tapering of dosage for those patients on medication for a prolonged period of time. Use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated patients, it is recommended that the dosage be limited to 15 mg to reduce risk of oversedation, dizziness, confusion and/or ataxia. Consider potential additive effects with other hypnotics or CNS depressants. Employ usual precautions in severely depressed patients, or in those with latent depression or suicidal tendencies, or in those with impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported: headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of leukopenia, granulocytopenia, sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins, and alkaline phosphatase; and paradoxical reactions, *e.g.*, excitement, stimulation and hyperactivity.

Dosage: Individualize for maximum beneficial effect. *Adults:* 30 mg usual dosage; 15 mg may suffice in some patients. *Elderly or debilitated patients:* 15 mg recommended initially until response is determined.

Supplied: Capsules containing 15 mg or 30 mg flurazepam HCl.

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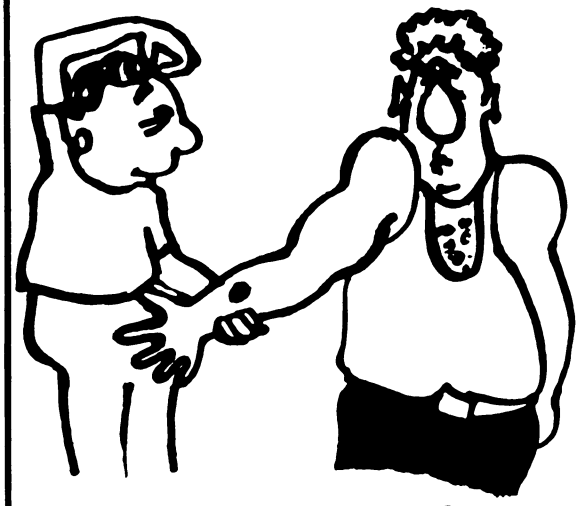

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SORBITRATE®
(ISOSORBIDE DINITRATE)

Please consult full prescribing information before use. A summary follows:

INDICATIONS AND USAGE: SORBITRATE (isosorbide dinitrate) is indicated for the treatment and prevention of angina pectoris. All dosage forms of isosorbide dinitrate may be used prophylactically to decrease frequency and severity of anginal attacks and can be expected to decrease the need for sublingual nitroglycerin.

The sublingual and chewable forms of the drug are indicated for acute prophylaxis of angina pectoris when taken a few minutes before situations likely to provoke anginal attacks. Because of a slower onset of effect, the oral forms of isosorbide dinitrate are not indicated for acute prophylaxis.

CONTRAINDICATIONS: SORBITRATE is contraindicated in patients who have shown purported hypersensitivity or idiosyncrasy to it or other nitrates or nitrites. Epinephrine and related compounds are ineffective in reversing the severe hypotensive events associated with overdose and are contraindicated in this situation.

WARNINGS: The benefits of SORBITRATE during the early days of an acute myocardial infarction have not been established. If one elects to use organic nitrates in early infarction, hemodynamic monitoring and frequent clinical assessment should be used because of the potential deleterious effects of hypotension.

PRECAUTIONS: General: Severe hypotensive response, particularly with upright posture, may occur with even small doses of SORBITRATE. The drug should therefore be used with caution in subjects who may have blood volume depletion from diuretic therapy or in subjects who have low systolic blood pressure (eg, below 90 mmHg). Paradoxical bradycardia and increased angina pectoris may accompany nitrate-induced hypotension. Nitrate therapy may aggravate the angina caused by hypertrophic cardiomyopathy.

Marked symptomatic, orthostatic hypotension has been reported when calcium channel blockers and organic nitrates were used in combination. Dose adjustment of either class of agents may be necessary.

Tolerance to this drug and cross-tolerance to other nitrates and nitrites may occur. Tolerance to the vascular and antianginal effects of isosorbide dinitrate or nitroglycerin has been demonstrated in clinical trials, experience through occupational exposure, and in isolated tissue experiments in the laboratory. The importance of tolerance to the appropriate use of isosorbide dinitrate in the management of patients with angina pectoris has not been determined. However, one clinical trial using treadmill exercise tolerance (as an end point) found an 8-hour duration of action of oral isosorbide dinitrate following the first dose (after a 2-week placebo washout) and only a 2-hour duration of effect of the same dose after 1 week of repetitive dosing at conventional dosing intervals. On the other hand, several trials have been able to differentiate isosorbide dinitrate from placebo after 4 weeks of therapy and, in open trials, an effect seems detectable for as long as several months.

Tolerance clearly occurs in industrial workers continuously exposed to nitroglycerin. Moreover, physical dependence also occurs since chest pain, acute myocardial infarction, and even sudden death have occurred during temporary withdrawal of nitroglycerin from the workers. In clinical trials in angina patients, there are reports of anginal attacks being more easily provoked and of rebound in the hemodynamic effects soon after nitrate withdrawal. The relative importance of these observations to the routine, clinical use of isosorbide dinitrate is not known. However, it seems prudent to gradually withdraw patients from isosorbide dinitrate when the therapy is being terminated, rather than stopping the drug abruptly.

Information for Patients: Headache may occur during initial therapy with SORBITRATE. Headache is usually relieved by the use of standard headache remedies or by lowering the dose and tends to disappear after the first week or two of use.

Drug Interactions: Alcohol may enhance any marked sensitivity to the hypotensive effect of nitrates.

Isosorbide dinitrate acts directly on vascular smooth muscle; therefore, any other agent that depends on vascular smooth muscle as the final common path can be expected to have decreased or increased effect depending on the agent.

Carcinogenesis, Mutagenesis, Impairment of Fertility: No long-term studies in animals have been performed to evaluate the carcinogenic potential of this drug. A modified two-litter reproduction study in rats fed isosorbide dinitrate at 25 or 100 mg/kg/day did not reveal any effects on fertility or gestation or any remarkable gross pathology in any parent or offspring fed isosorbide dinitrate as compared with rats fed a basal-controlled diet.

Pregnancy Category C: Isosorbide dinitrate has been shown to cause a dose-related increase in embryotoxicity (increase in mummified pups) in rabbits at oral doses 35 and 150 times the maximum recommended human daily dose. There are no adequate and well-controlled studies in pregnant women. SORBITRATE should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when SORBITRATE is administered to a nursing woman.

Pediatric Use: The safety and effectiveness of SORBITRATE in children has not been established.

ADVERSE REACTIONS: Adverse reactions, particularly headache and hypotension, are dose-related. In clinical trials at various doses, the following have been observed:

Headache is the most common (reported incidence varies widely, apparently being dose-related, with an average occurrence of about 25%) adverse reaction and may be severe and persistent. Cutaneous vasodilation with flushing may occur. Transient episodes of dizziness and weakness, as well as other signs of cerebral ischemia associated with postural hypotension, may occasionally develop (the incidence of reported symptomatic hypotension ranges from 2% to 36%). An occasional individual will exhibit marked sensitivity to the hypotensive effects of nitrates and severe responses (nausea, vomiting, weakness, restlessness, pallor, perspiration, and collapse) may occur even with the usual therapeutic dose. Drug rash and/or exfoliative dermatitis may occasionally occur. Nausea and vomiting appear to be uncommon. Case reports of clinically significant methemoglobinemia are rare at conventional doses of organic nitrates. The formation of methemoglobin is dose-related and, in the case of genetic abnormalities of hemoglobin that favor methemoglobin formation, even conventional doses of organic nitrate could produce harmful concentrations of methemoglobin.

DOSAGE AND ADMINISTRATION: For the treatment of angina pectoris, the usual starting dose for sublingual SORBITRATE is 2.5 to 5 mg; for chewable tablets, 5 mg; for oral (swallowed) tablets, 5 to 20 mg, and for controlled-release forms, 40 mg.

SORBITRATE should be titrated upward until angina is relieved or side effects limit the dose. In ambulatory patients, the magnitude of the incremental dose increase should be guided by measurements of standing blood pressure.

The initial dosage of sublingual or chewable SORBITRATE for prophylactic therapy in angina pectoris patients is generally 5 or 10 mg every 2 to 3 hours. Adequate controlled clinical studies demonstrating the effectiveness of chronic maintenance therapy with these dosage forms have not been reported.

SORBITRATE in oral doses of 10 to 40 mg given every 6 hours or in oral controlled-release doses of 40 to 80 mg given every 8 to 12 hours is generally recommended. The extent to which development of tolerance should modify the dosage program has not been defined. *The oral controlled-release forms of isosorbide dinitrate should not be chewed.*

DOSAGE FORMS AVAILABLE: Sublingual Tablets (2.5, 5, 10 mg). Chewable Tablets (5, 10 mg). Oral Tablets (5, 10, 20, 30, 40 mg). Sustained Action Tablets (40 mg).

STUART PHARMACEUTICALS
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See following page.

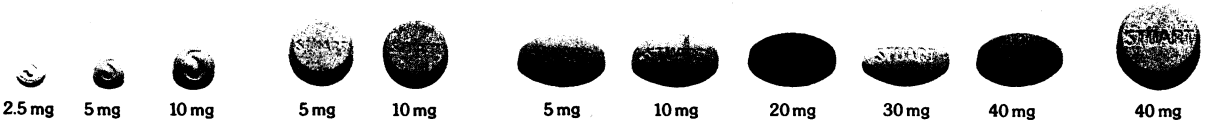
Angina comes in many forms...

So does

SORBITRATE®

(ISOSORBIDE DINITRATE)

Unsurpassed flexibility in nitrate therapy.



2.5 mg 5 mg 10 mg
Sublingual Tablets

5 mg 10 mg
Chewable Tablets

5 mg 10 mg 20 mg 30 mg 40 mg
Oral "Swallow" Tablets

40 mg
Sustained Action "Swallow" Tablets

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See previous page for brief summary of prescribing information.

ACE* INHIBITOR

Capoten®
(captopril tablets)

Precautionary Guidelines

CAPOTEN has been associated with the development of neutropenia/agranulocytosis (0.3% of 4,000 patients) or proteinuria (1.2% of 4,000 patients).† These serious side effects are more likely to occur in patients with predisposing conditions, such as renal impairment or autoimmune disease, or in patients receiving therapy known to suppress the autoimmune response.

The following precautionary guidelines are recommended for all patients receiving CAPOTEN:

☐ Obtain urinary protein level estimates prior to initiating therapy, at monthly intervals for the first nine months of treatment, and periodically thereafter.

☐ Obtain WBC counts at the initiation of therapy, at two-week intervals for the first three months of treatment, and periodically thereafter.

☐ Carefully review the WARNINGS and ADVERSE REACTIONS sections in the complete prescribing information, with particular attention to the patient at increased risk.

☐ The most frequently occurring adverse reactions are skin rash and taste alteration; both effects are generally mild, reversible, or self-limited.

*Angiotensin Converting Enzyme

†Please see the following brief summary of prescribing information for INDICATIONS AND USAGE, WARNINGS, and ADVERSE REACTIONS.

Reference: 1. Market Measures Inc.: Treatment of Hypertension V, February 1983.

CAPOTEN® TABLETS
Captopril Tablets

INDICATIONS: Hypertension—Because serious adverse effects have been reported (see WARNINGS), CAPOTEN is indicated for treatment of hypertensive patients who on multidrug regimens have either failed to respond satisfactorily or developed unacceptable side effects.

Heart Failure: CAPOTEN (captopril) is indicated in patients with heart failure who have not responded adequately to or cannot be controlled by conventional diuretic and digitalis therapy. CAPOTEN is to be used with diuretics and digitalis.

WARNINGS: Proteinuria—Total urinary proteins >1 g/day were seen in 1.2% of patients on captopril; the nephrotic syndrome occurred in about ¼th of these cases. About 60% of affected patients had evidence of prior renal disease; the remainder had no known renal dysfunction. In most cases, proteinuria subsided or cleared within 6 months whether or not captopril was continued. The BUN and creatinine were seldom altered in proteinuric patients.

Membranous glomerulopathy was found in nearly all the proteinuric patients on captopril who were biopsied and may be drug related. Most cases of proteinuria occurred by the 8th month of therapy. Patients should have urinary protein estimates (dip-stick on 1st morning urine, or quantitative 24-hr urine—the latter provides greater precision when proteinuria is persistent and/or at low levels) before therapy, at approx. monthly intervals for the 1st 9 months of therapy, and periodically thereafter. For patients who develop proteinuria >1 g/day, or increasing proteinuria, the benefits and risks of continuing captopril should be evaluated.

Neutropenia/Agranulocytosis—Neutropenia (<300/mm³) associated with myeloid hypoplasia (probably drug related) occurred in about 0.3% of captopril treated patients. About half of the neutropenic patients developed systemic or oral cavity infections or other features of agranulocytosis. Most of the neutropenic patients had severe hypertension and renal function impairment; about half had systemic lupus erythematosus (SLE), or another autoimmune/collagen disorder; multiple concomitant drug therapy was common, including immunosuppressive therapy in a few cases. Daily doses of captopril in the leukopenic patients were relatively high, particularly in view of their diminished renal function. The neutropenia appeared 3 to 12 weeks after starting captopril; it developed relatively slowly, taking 10 to 30 days to have white blood count fall to its nadir; neutrophils returned to normal in about 2 weeks (other than 2 patients who died of sepsis).

Use captopril with caution in patients with impaired renal function, serious autoimmune disease (particularly SLE), or who are exposed to other drugs known to affect the white cells or immune response. In patients at particular risk (as noted above), perform white blood cell and differential counts prior to therapy, at about 2-week intervals for about the 1st 3 months of therapy, and periodically thereafter.

The risk of neutropenia in patients who are less seriously ill or who receive lower dosages appears to be smaller. In these patients white blood cell counts should be performed every 2 weeks for the 1st 3 months of therapy, and periodically thereafter. Perform differential counts when leukocytes are <4000/mm³ or the pretherapy white count is halved. All patients treated with captopril should be told to report any signs of infection (e.g., sore throat; fever); if infection is suspected, perform counts without delay. Since discontinuation of captopril and other drugs has generally led to prompt return of the white count to normal, upon confirmation of neutropenia (neutrophil count <1000/mm³) withdraw captopril and closely follow the patient's course.

Hypotension—Excessive hypotension was rarely seen in hypertensive patients but is a possibility in severely salt/volume-depleted persons such as those treated vigorously with diuretics (see PRECAUTIONS [Drug Interactions]).

In heart failure, where blood pressure was either normal or low, transient decreases in blood pressure >20% were recorded in about ½ the patients. This transient hypotension may occur after any of the first several doses and is usually well tolerated, although rarely it has been associated with arrhythmia or conduction defects. A starting dose of 6.25 or 12.5 mg tid may minimize the hypotensive effect. Patients should be followed closely for the first 2 weeks of treatment and whenever the dose of captopril and/or diuretic is increased.

BECAUSE OF THE POTENTIAL FALL IN BLOOD PRESSURE IN THESE PATIENTS, THERAPY SHOULD BE STARTED UNDER VERY CLOSE MEDICAL SUPERVISION.

PRECAUTION: General: *Impaired Renal Function,* Hypertension—Some hypertensive patients with renal disease, particularly those with severe renal artery stenosis, have developed increases in BUN and serum creatinine. It may be necessary to reduce captopril dosage and/or discontinue diuretic. For some of these patients, normalization of blood pressure and maintenance of adequate renal perfusion may not be possible. Heart Failure—About 20% of patients develop stable elevations of BUN and serum creatinine >20% above normal or baseline upon long-term treatment. Less than 5% of patients, generally with severe preexisting renal disease, required discontinuation due to progressively increasing creatinine. See DOSAGE AND ADMINISTRATION, ADVERSE REACTIONS [Altered Laboratory Findings]. *Valvular Stenosis*—A theoretical concern, for risk of decreased coronary perfusion, has been noted regarding vasodilator treatment in patients with aortic stenosis, due to decreased afterload reduction.

Surgery/Anesthesia—If hypotension occurs during major surgery or anesthesia, and is considered due to the effects of captopril, it is correctable by volume expansion.

Drug Interactions: *Hypotension: Patients on Diuretic Therapy*—Precipitous reduction of blood pressure may occasionally occur within the 1st 3 hours after administration of the initial captopril dose in patients on diuretics, especially those recently placed on diuretics and those on severe dietary salt restriction or dialysis. This possibility can be minimized by either discontinuing the diuretic or increasing the salt intake about 1 week prior to initiation of captopril therapy. Alternatively, provide medical supervision for at least 3 hours after the initial dose in hypertensive patients.

Agents Having Vasodilator Activity: In heart failure patients vasodilators should be administered with caution.

Agents Causing Renin Release—Captopril's effect will be augmented by antihypertensive agents that cause renin release.

Agents Affecting Sympathetic Activity—The sympathetic nervous system may be especially important in supporting blood pressure in patients receiving captopril alone or with diuretics. Beta-adrenergic blocking drugs add some further antihypertensive effect to captopril, but the overall response is less than additive. Therefore, use agents affecting sympathetic activity (e.g., ganglionic blocking agents or adrenergic neuron blocking agents) with caution.

Agents Increasing Serum Potassium—Give potassium-sparing diuretics or potassium supplements only for documented hypokalemia, and then with caution, since they may lead to a significant increase of serum potassium.

Drug/Laboratory Test Interaction: Captopril may cause a false-positive urine test for acetone.

Carcinogenesis, Mutagenesis, and Impairment of Fertility: Two-year studies with doses of 50 to 1350 mg/kg/day in mice and rats failed to show any evidence of carcinogenic potential. Studies in rats have revealed no impairment of fertility.

Usage in Pregnancy: There are no adequate and well-controlled studies in pregnant women. Embryocidal effects were observed in rabbits. Therefore, captopril should be used during pregnancy only if the potential benefit outweighs the potential risk to the fetus.

(Continued on adjacent page)

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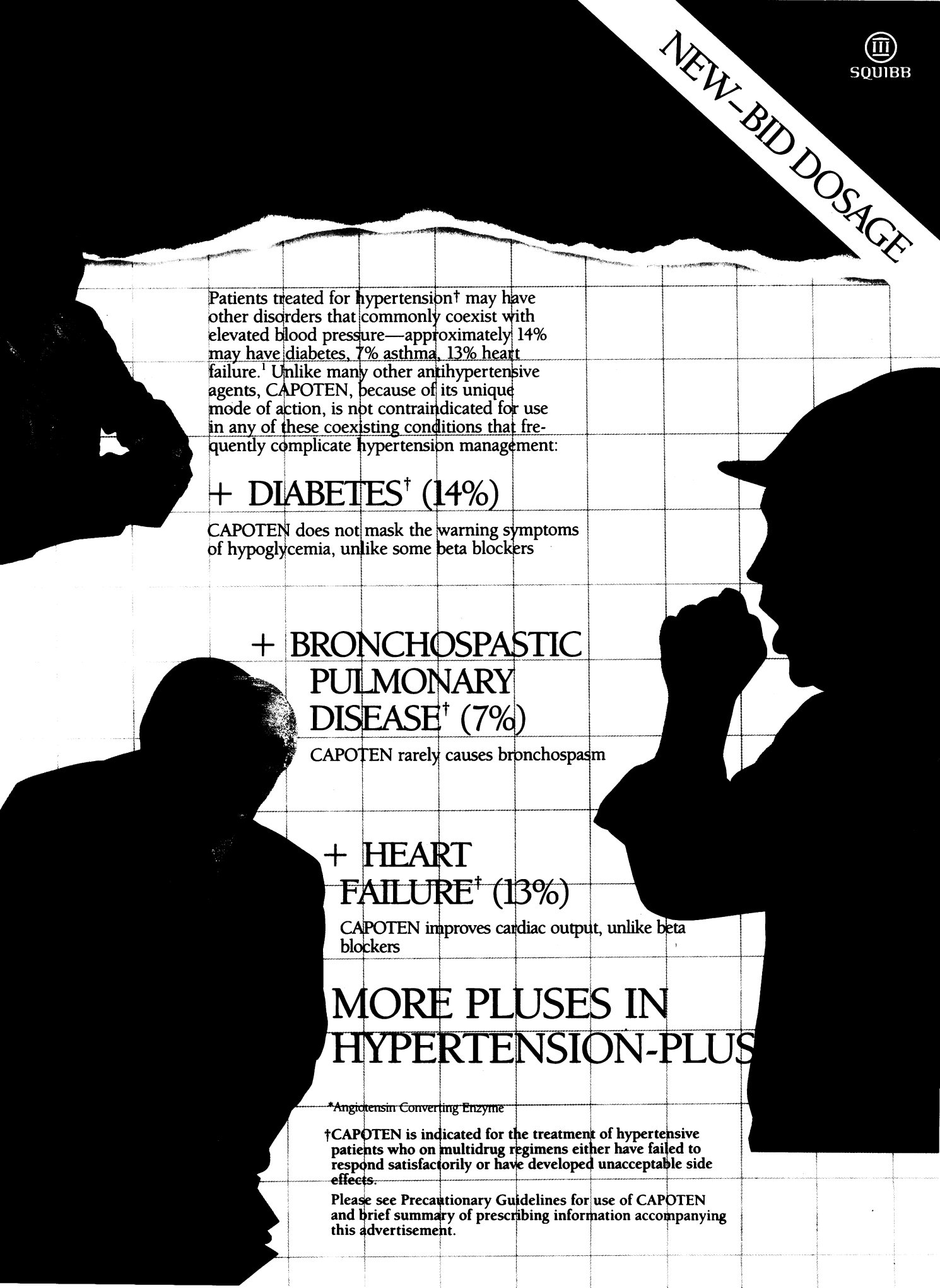
NEW-BID DOSAGE
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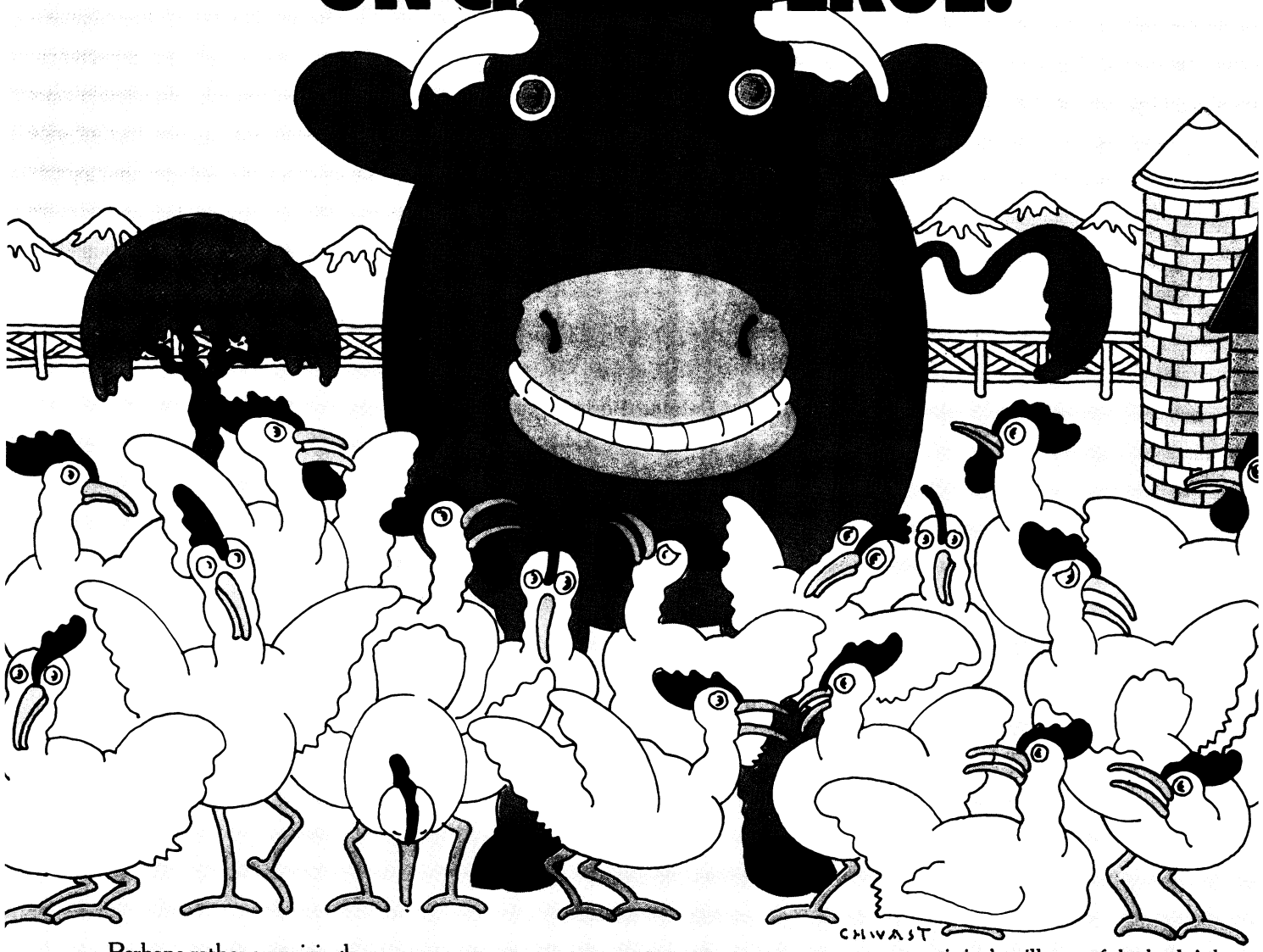
Patients treated for hypertension† may have other disorders that commonly coexist with elevated blood pressure—approximately 14% may have diabetes, 7% asthma, 13% heart failure.[1] Unlike many other antihypertensive agents, CAPOTEN, because of its unique mode of action, is not contraindicated for use in any of these coexisting conditions that frequently complicate hypertension management:
+ DIABETES† (14%)
CAPOTEN does not mask the warning symptoms of hypoglycemia, unlike some beta blockers
+ BRONCHOSPASTIC PULMONARY DISEASE† (7%)
CAPOTEN rarely causes bronchospasm
+ HEART FAILURE† (13%)
CAPOTEN improves cardiac output, unlike beta blockers
MORE PLUSES IN HYPERTENSION-PLUS
*Angiotensin Converting Enzyme
†CAPOTEN is indicated for the treatment of hypertensive patients who on multidrug regimens either have failed to respond satisfactorily or have developed unacceptable side effects.
Please see Precautionary Guidelines for use of CAPOTEN and brief summary of prescribing information accompanying this advertisement.

ANNOUNCING SOME NEW FINDINGS ON CHOLESTEROL.



Perhaps rather surprisingly, beef has no more cholesterol than chicken. Even roast chicken without skin.

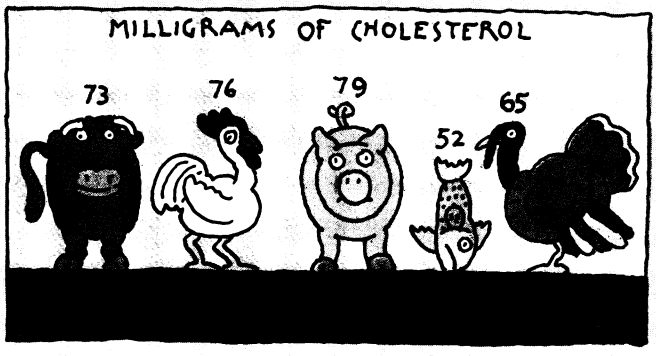
That was the finding of a new U.S.D.A. study on beef nutrient composition.*

That same study found beef is lower in calories than ever.

And lower in fat.

In fact, three ounces of beef now has just 192 calories and a modest nine grams of fat, over half of which is unsaturated.

Today, new breeding and feeding techniques are making beef a whole different animal. Though not so different that it isn't still one of the body's best sources of iron, zinc, B-vitamins and protein.



It all means moderate portions of beef can fit easily into a reduced cholesterol, low saturated fat diet.

And that can stop a lot of squawking when you recommend one.

For more information on the new U.S.D.A. study and beef's contribution to healthy eating in the eighties, write to Beef Nutrition, California Beef Council, 551 Foster City Boulevard, Suite A, Foster City, California 94404.

*Beef data from 1983 Beef Nutritive Composition Studies conducted by the U.S.D.A. and National Live Stock and Meat Board.

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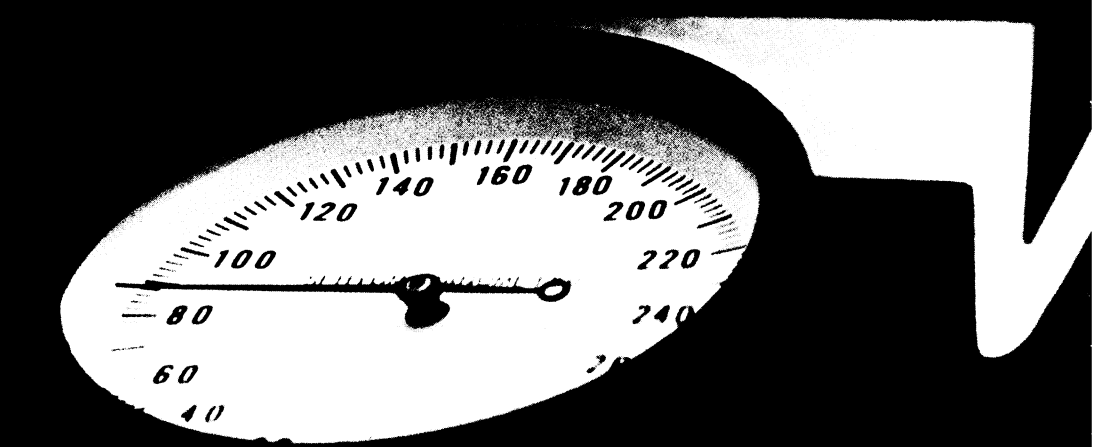
Right from the start in hypertension...



Once-daily INDERAL LA (propranolol HCl) for smooth blood pressure control without the potassium problems of diuretics

Once-daily INDERAL LA (propranolol HCl) avoids the risk of diuretic-induced ECG abnormalities due to hypokalemia.[1-4] In addition, INDERAL LA preserves potassium balance without additive agents or supplements while providing simple, well-tolerated therapy with broad cardiovascular benefits.

Once-daily INDERAL LA for the cardiovascular benefits of the world's leading beta blocker

Simply start with 80 mg once daily. Dosage may be increased to 120 mg to 160 mg once daily as needed to achieve additional control.

Like conventional INDERAL tablets, INDERAL LA should not be used in the presence of congestive heart failure, sinus bradycardia, heart block greater than first degree, and bronchial asthma.

The appearance of these capsules is a registered trademark of Ayerst Laboratories.

80 mg 120 mg 160 mg

Please see brief summary of prescribing information on the next page for further details.

Once-daily
For beta-1/beta-2 blockade INDERAL® LA
(PROPRANOLOL HCl) LONG ACTING CAPSULES

The appearance of these capsules is a registered trademark of Ayerst Laboratories.

BRIEF SUMMARY *(FOR FULL PRESCRIBING INFORMATION, SEE PACKAGE CIRCULAR.)*
INDERAL® LA brand of propranolol hydrochloride **(Long Acting Capsules)**
DESCRIPTION. Inderal LA is formulated to provide a sustained release of propranolol hydrochloride. Inderal LA is available as 80 mg, 120 mg, and 160 mg capsules.
CLINICAL PHARMACOLOGY. INDERAL is a nonselective beta-adrenergic receptor blocking agent possessing no other autonomic nervous system activity. It specifically competes with beta-adrenergic receptor stimulating agents for available receptor sites. When access to beta-receptor sites is blocked by INDERAL, the chronotropic, inotropic, and vasodilator responses to beta-adrenergic stimulation are decreased proportionately.

INDERAL LA Capsules (80, 120, and 160 mg) release propranolol HCl at a controlled and predictable rate. Peak blood levels following dosing with INDERAL LA occur at about 6 hours and the apparent plasma half-life is about 10 hours. When measured at steady state over a 24-hour period the areas under the propranolol plasma concentration-time curve (AUCs) for the capsules are approximately 60% to 65% of the AUCs for a comparable divided daily dose of INDERAL tablets. The lower AUCs for the capsules are due to greater hepatic metabolism of propranolol, resulting from the slower rate of absorption of propranolol. Over a twenty-four (24) hour period, blood levels are fairly constant for about twelve (12) hours then decline exponentially.

INDERAL LA should not be considered a simple mg for mg substitute for conventional propranolol and the blood levels achieved do not match (are lower than) those of two to four times daily dosing with the same dose. When changing to INDERAL LA from conventional propranolol, a possible need for retitration upwards should be considered especially to maintain effectiveness at the end of the dosing interval. In most clinical settings, however, such as hypertension or angina where there is little correlation between plasma levels and clinical effect, INDERAL LA has been therapeutically equivalent to the same mg dose of conventional INDERAL as assessed by 24-hour effects on blood pressure and on 24-hour exercise responses of heart rate, systolic pressure and rate pressure product. INDERAL LA can provide effective beta blockade for a 24-hour period.

The mechanism of the antihypertensive effect of INDERAL has not been established. Among the factors that may be involved in contributing to the antihypertensive action are (1) decreased cardiac output, (2) inhibition of renin release by the kidneys, and (3) diminution of tonic sympathetic nerve outflow from vasomotor centers in the brain. Although total peripheral resistance may increase initially, it readjusts to or below the pretreatment level with chronic use. Effects on plasma volume appear to be minor and somewhat variable. INDERAL has been shown to cause a small increase in serum potassium concentration when used in the treatment of hypertensive patients.

In angina pectoris, propranolol generally reduces the oxygen requirement of the heart at any given level of effort by blocking the catecholamine-induced increases in the heart rate, systolic blood pressure, and the velocity and extent of myocardial contraction. Propranolol may increase oxygen requirements by increasing left ventricular fiber length, end diastolic pressure and systolic ejection period. The net physiologic effect of beta-adrenergic blockade is usually advantageous and is manifested during exercise by delayed onset of pain and increased work capacity.

In dosages greater than required for beta blockade, INDERAL also exerts a quinidine-like or anesthetic-like membrane action which affects the cardiac action potential. The significance of the membrane action in the treatment of arrhythmias is uncertain.

The mechanism of the antimigraine effect of propranolol has not been established. Beta-adrenergic receptors have been demonstrated in the pial vessels of the brain.

Beta receptor blockade can be useful in conditions in which, because of pathologic or functional changes, sympathetic activity is detrimental to the patient. But there are also situations in which sympathetic stimulation is vital. For example, in patients with severely damaged hearts, adequate ventricular function is maintained by virtue of sympathetic drive which should be preserved. In the presence of AV block, greater than first degree, beta blockade may prevent the necessary facilitating effect of sympathetic activity on conduction. Beta blockade results in bronchial constriction by interfering with adrenergic bronchodilator activity which should be preserved in patients subject to bronchospasm.

Propranolol is not significantly dialyzable.
INDICATIONS AND USAGE. Hypertension: INDERAL LA is indicated in the management of hypertension; it may be used alone or used in combination with other antihypertensive agents, particularly a thiazide diuretic. INDERAL LA is not indicated in the management of hypertensive emergencies.

Angina Pectoris Due to Coronary Atherosclerosis: INDERAL LA is indicated for the long-term management of patients with angina pectoris.

Migraine: INDERAL LA is indicated for the prophylaxis of common migraine headache. The efficacy of propranolol in the treatment of a migraine attack that has started has not been established and propranolol is not indicated for such use.

Hypertrophic Subaortic Stenosis: INDERAL LA is useful in the management of hypertrophic subaortic stenosis, especially for treatment of exertional or other stress-induced angina, palpitations, and syncope. INDERAL LA also improves exercise performance. The effectiveness of propranolol hydrochloride in this disease appears to be due to a reduction of the elevated outflow pressure gradient which is exacerbated by beta-receptor stimulation. Clinical improvement may be temporary.
CONTRAINDICATIONS. INDERAL is contraindicated in 1) cardiogenic shock; 2) sinus bradycardia and greater than first degree block; 3) bronchial asthma; 4) congestive heart failure (see WARNINGS) unless the failure is secondary to a tachyarrhythmia treatable with INDERAL.
WARNINGS. CARDIAC FAILURE: Sympathetic stimulation may be a vital component supporting circulatory function in patients with congestive heart failure, and its inhibition by beta blockade may precipitate more severe failure. Although beta blockers should be avoided in overt congestive heart failure, if necessary, they can be used with close follow-up in patients with a history of failure who are well compensated and are receiving digitalis and diuretics. Beta-adrenergic blocking agents do not abolish the inotropic action of digitalis on heart muscle.

IN PATIENTS WITHOUT A HISTORY OF HEART FAILURE, continued use of beta blockers can, in some cases, lead to cardiac failure. Therefore, at the first sign or symptom of heart failure, the patient should be digitalized and/or treated with diuretics, and the response observed closely, or INDERAL should be discontinued (gradually, if possible).

IN PATIENTS WITH ANGINA PECTORIS, there have been reports of exacerbation of angina and, in some cases, myocardial infarction, following abrupt discontinuance of INDERAL therapy. Therefore, when discontinuance of INDERAL is planned the dosage should be gradually reduced over at least a few weeks, and the patient should be cautioned against interruption or cessation of therapy without the physician's advice. If INDERAL therapy is interrupted and exacerbation of angina occurs, it usually is advisable to reinstitute INDERAL therapy and take other measures appropriate for the management of unstable angina pectoris. Since coronary artery disease may be unrecognized, it may be prudent to follow the above advice in patients considered at risk of having occult atherosclerotic heart disease who are given propranolol for other indications.

Nonallergic Bronchospasm (e.g., chronic bronchitis, emphysema)— PATIENTS WITH BRONCHOSPASTIC DISEASES SHOULD IN GENERAL NOT RECEIVE BETA BLOCKERS. INDERAL should be administered with caution since it may block bronchodilation produced by endogenous and exogenous catecholamine stimulation of beta receptors.

MAJOR SURGERY: The necessity or desirability of withdrawal of beta-blocking therapy prior to major surgery is controversial. It should be noted, however, that the impaired ability of the heart to respond to reflex adrenergic stimuli may augment the risks of general anesthesia and surgical procedures.

INDERAL (propranolol HCl), like other beta blockers, is a competitive inhibitor of beta-receptor agonists and its effects can be reversed by administration of such agents, e.g., dobutamine or isoproterenol. However, such patients may be subject to protracted severe hypotension. Difficulty in starting and maintaining the heartbeat has also been reported with beta blockers.

DIABETES AND HYPOGLYCEMIA: Beta-adrenergic blockade may prevent the appearance of certain premonitory signs and symptoms (pulse rate and pressure changes) of acute hypoglycemia in labile insulin-dependent diabetes. In these patients, it may be more difficult to adjust the dosage of insulin.

THYROTOXICOSIS: Beta blockade may mask certain clinical signs of hyperthyroidism. Therefore, abrupt withdrawal of propranolol may be followed by an exacerbation of symptoms of hyperthyroidism, including thyroid storm. Propranolol does not distort thyroid function tests.

IN PATIENTS WITH WOLFF-PARKINSON-WHITE SYNDROME, several cases have been reported in which, after propranolol, the tachycardia was replaced by a severe bradycardia requiring a demand pacemaker. In one case this resulted after an initial dose of 5 mg propranolol.
PRECAUTIONS. *General:* Propranolol should be used with caution in patients with impaired hepatic or renal function. INDERAL (propranolol HCl) is not indicated for the treatment of hypertensive emergencies.

Beta adrenoreceptor blockade can cause reduction of intraocular pressure. Patients should be told that INDERAL may interfere with the glaucoma screening test. Withdrawal may lead to a return of increased intraocular pressure.

Clinical Laboratory Tests: Elevated blood urea levels in patients with severe heart disease, elevated serum transaminase, alkaline phosphatase, lactate dehydrogenase.

DRUG INTERACTIONS: Patients receiving catecholamine-depleting drugs such as reserpine should be closely observed if INDERAL is administered. The added catecholamine-blocking action may produce an excessive reduction of resting sympathetic nervous activity which may result in hypotension, marked bradycardia, vertigo, syncopal attacks, or orthostatic hypotension.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term studies in animals have been conducted to evaluate toxic effects and carcinogenic potential. In 18-month studies in both rats and mice, employing doses up to 150 mg/kg/day, there was no evidence of significant drug-induced toxicity. There were no drug-related tumorigenic effects at any of the dosage levels. Reproductive studies in animals did not show any impairment of fertility that was attributable to the drug.

Pregnancy: Pregnancy Category C. INDERAL has been shown to be embryotoxic in animal studies at doses about 10 times greater than the maximum recommended human dose.

There are no adequate and well-controlled studies in pregnant women. INDERAL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: INDERAL is excreted in human milk. Caution should be exercised when INDERAL is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in children have not been established.
ADVERSE REACTIONS. Most adverse effects have been mild and transient and have rarely required the withdrawal of therapy.

Cardiovascular: bradycardia; congestive heart failure; intensification of AV block; hypotension; paresthesia of hands; thrombocytopenic purpura; arterial insufficiency, usually of the Raynaud type.

Central Nervous System: lightheadedness; mental depression manifested by insomnia, lassitude, weakness, fatigue; reversible mental depression progressing to catatonia; visual disturbances; hallucinations; an acute reversible syndrome characterized by disorientation for time and place, short-term memory loss, emotional lability, slightly clouded sensorium, and decreased performance on neuropsychometrics.

Gastrointestinal: nausea, vomiting, epigastric distress, abdominal cramping, diarrhea, constipation, mesenteric arterial thrombosis, ischemic colitis.

Allergic: pharyngitis and agranulocytosis, erythematous rash, fever combined with aching and sore throat, laryngospasm and respiratory distress.

Respiratory: bronchospasm.

Hematologic: agranulocytosis, nonthrombocytopenic purpura, thrombocytopenic purpura.

Auto-Immune: In extremely rare instances, systemic lupus erythematosus has been reported.

Miscellaneous: alopecia, LE-like reactions, psoriasiform rashes, dry eyes, male impotence, and Peyronie's disease have been reported rarely. Oculomucocutaneous reactions involving the skin, serous membranes and conjunctivae reported for a beta blocker (practolol) have not been associated with propranolol.
DOSAGE AND ADMINISTRATION. INDERAL LA provides propranolol hydrochloride in a sustained-release capsule for administration once daily. If patients are switched from INDERAL tablets to INDERAL LA capsules, care should be taken to assure that the desired therapeutic effect is maintained. INDERAL LA should not be considered a simple mg for mg substitute for INDERAL. INDERAL LA has different kinetics and produces lower blood levels. Retitration may be necessary especially to maintain effectiveness at the end of the 24-hour dosing interval.

HYPERTENSION—*Dosage must be individualized.* The usual initial dosage is 80 mg INDERAL LA once daily, whether used alone or added to a diuretic. The dosage may be increased to 120 mg once daily or higher until adequate blood pressure control is achieved. The usual maintenance dosage is 120 to 160 mg once daily. In some instances a dosage of 640 mg may be required. The time needed for full hypertensive response to a given dosage is variable and may range from a few days to several weeks.

ANGINA PECTORIS—*Dosage must be individualized.* Starting with 80 mg INDERAL LA once daily, dosage should be gradually increased at three to seven day intervals until optimum response is obtained. Although individual patients may respond at any dosage level, the average optimum dosage appears to be 160 mg once daily. In angina pectoris, the value and safety of dosage exceeding 320 mg per day have not been established.

If treatment is to be discontinued, reduce dosage gradually over a period of a few weeks (see WARNINGS).

MIGRAINE—*Dosage must be individualized.* The initial oral dose is 80 mg INDERAL LA once daily. The usual effective dose range is 160-240 mg once daily. The dosage may be increased gradually to achieve optimum migraine prophylaxis. If a satisfactory response is not obtained within four to six weeks after reaching the maximum dose, INDERAL LA therapy should be discontinued. It may be advisable to withdraw the drug gradually over a period of several weeks.

HYPERTROPHIC SUBAORTIC STENOSIS—80-160 mg INDERAL LA once daily.

PEDIATRIC DOSAGE—At this time the data on the use of the drug in this age group are too limited to permit adequate directions for use.

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1. Holland OB, Nixon JV, Kuhnert L: Diuretic-induced ventricular ectopic activity. *Am J Med* 1981;70:762-768. **2.** Holme I, Helgeland A, Hjermann I, et al: Treatment of mild hypertension with diuretics. The importance of ECG abnormalities in the Oslo study and in MRFIT. *JAMA* 1984;251:1298-1299.

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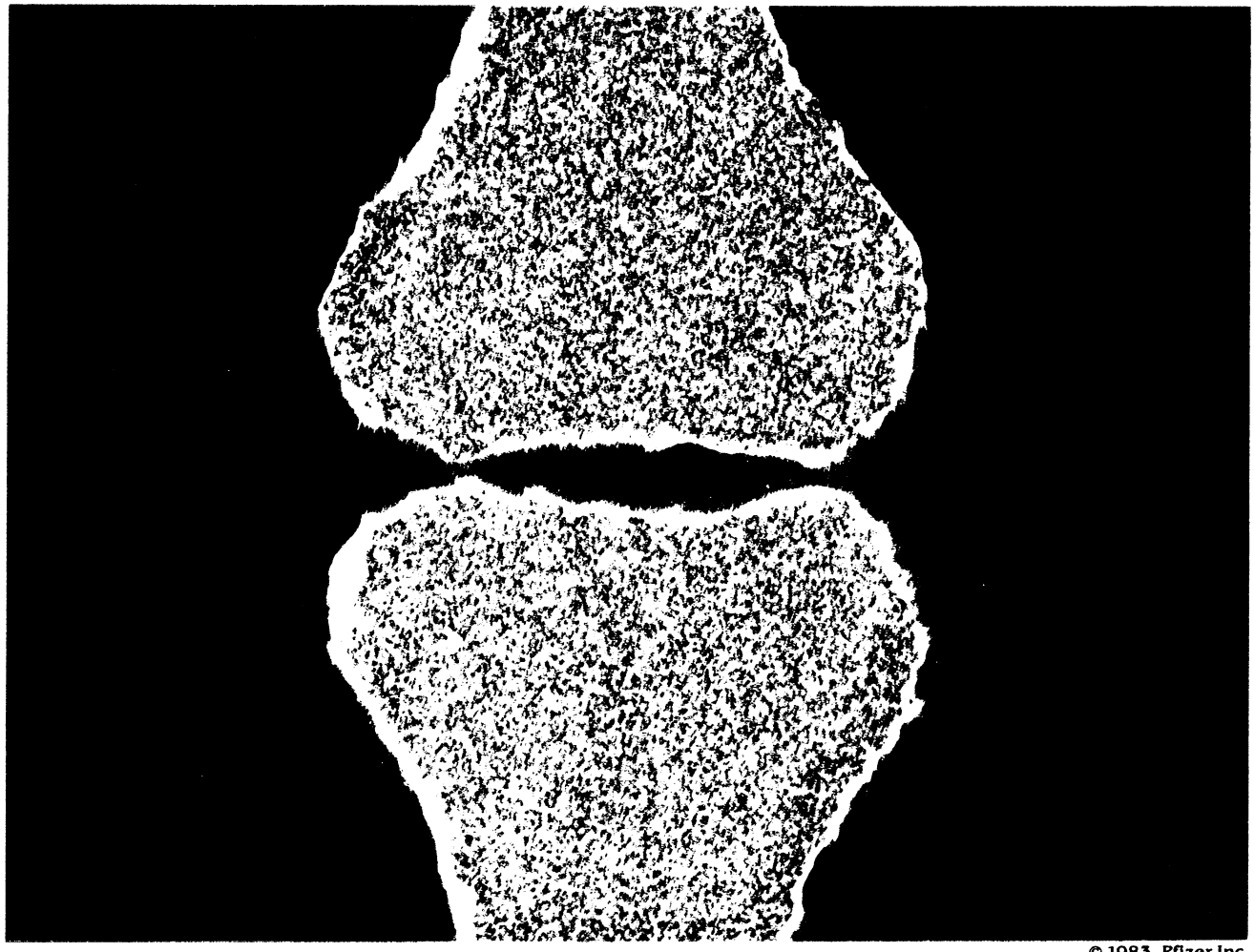

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This is how an arthritis patient's joints often feel.

You can help these patients feel better with one-a-day FELDENE (piroxicam).
For good reasons:

- it's effective—proven relief of the pain and inflammation of rheumatoid arthritis and osteoarthritis in millions of patients, in 80 countries all around the world.
- it's efficient—once daily, 20-mg dose provides round-the-clock relief, improves compliance and remains effective during long-term therapy, maintaining 24-hour therapeutic blood levels once steady state is reached in 7 to 12 days.

Feldene® *ONE-A-DAY*

(PIROXICAM) 20 mg capsules

Please see FELDENE (piroxicam) prescribing information on the following page.

Feldene®
(PIROXICAM) 20 mg capsules

Prescribing Information

FELDENE® (piroxicam) Capsules *For Oral Use*

DESCRIPTION FELDENE (piroxicam) is 4-Hydroxy-2-methyl-*N*-2-pyridinyl-2*H*-1,2-benzothiazine-3-carboxamide 1,1-dioxide, an oxicam. Members of the oxicam family are not carboxylic acids, but they are acidic by virtue of the enolic 4-hydroxy substituent. FELDENE occurs as a white crystalline solid, sparingly soluble in water, dilute acid and most organic solvents. It is slightly soluble in alcohols and in aqueous alkaline solution. It exhibits a weakly acidic 4-hydroxy proton (pKa 5.1) and a weakly basic pyridyl nitrogen (pKa 1.8).

CLINICAL PHARMACOLOGY FELDENE has shown anti-inflammatory, analgesic and antipyretic properties in animals. Edema, erythema, tissue proliferation, fever, and pain can all be inhibited in laboratory animals by the administration of FELDENE. It is effective regardless of the etiology of the inflammation. The mode of action of FELDENE is not fully established at this time. However, a common mechanism for the above effects may exist in the ability of FELDENE to inhibit the biosynthesis of prostaglandins, known mediators of inflammation.

It is established that FELDENE does not act by stimulating the pituitary-adrenal axis.

FELDENE is well absorbed following oral administration. Drug plasma concentrations are proportional for 10 and 20 mg doses, generally peak within three to five hours after medication, and subsequently decline with a mean half-life of 50 hours (range of 30 to 86 hours, although values outside of this range have been encountered).

This prolonged half-life results in the maintenance of relatively stable plasma concentrations throughout the day on once daily doses and to significant drug accumulation upon multiple dosing. A single 20 mg dose generally produces peak piroxicam plasma levels of 1.5 to 2 mcg/ml, while maximum drug plasma concentrations, after repeated daily ingestion of 20 mg FELDENE, usually stabilize at 3-8 mcg/ml. Most patients approximate steady state plasma levels within 7 to 12 days. Higher levels, which approximate steady state at two to three weeks, have been observed in patients in whom longer plasma half-lives of piroxicam occurred.

FELDENE and its biotransformation products are excreted in urine and feces, with about twice as much appearing in the urine as the feces. Metabolism occurs by hydroxylation at the 5 position of the pyridyl side chain and conjugation of this product; by cyclodehydration; and by a sequence of reactions involving hydrolysis of the amide linkage, decarboxylation, ring contraction, and N-demethylation. Less than 5% of the daily dose is excreted unchanged.

Concurrent administration of aspirin (3900 mg/day) and FELDENE (20 mg/day), resulted in a reduction of plasma levels of piroxicam to about 80% of their normal values. The use of FELDENE in conjunction with aspirin is not recommended because data are inadequate to demonstrate that the combination produces greater improvement than that achieved with aspirin alone and the potential for adverse reactions is increased. Concomitant administration of antacids had no effect on FELDENE plasma levels. The effects of impaired renal function or hepatic disease on plasma levels have not been established.

FELDENE, like salicylates and other nonsteroidal anti-inflammatory agents, is associated with symptoms of gastrointestinal tract irritation (see ADVERSE REACTIONS). However, in a study utilizing ^{51}Cr-tagged red blood cells, 20 mg of FELDENE administered as a single dose for four days did not result in a significant increase in fecal blood loss and did not detectably affect the gastric mucosa. In the same study a total daily dose of 3900 mg of aspirin, i.e., 972 mg q.i.d., caused a significant increase in fecal blood loss and mucosal lesions as demonstrated by gastroscopy.

In controlled clinical trials, the effectiveness of FELDENE has been established for both acute exacerbations and long-term management of rheumatoid arthritis and osteoarthritis.

The therapeutic effects of FELDENE are evident early in the treatment of both diseases with a progressive increase in response over several (8-12) weeks. Efficacy is seen in terms of pain relief and, when present, subsidence of inflammation.

Doses of 20 mg/day FELDENE display a therapeutic effect comparable to therapeutic doses of aspirin, with a lower incidence of minor gastrointestinal effects and tinnitus.

FELDENE has been administered concomitantly with fixed doses of gold and corticosteroids. The existence of a "steroid-sparing" effect has not been adequately studied to date.

INDICATIONS AND USAGE FELDENE is indicated for acute or long-term use in the relief of signs and symptoms of the following:

1. osteoarthritis
2. rheumatoid arthritis

Dosage recommendations for use in children have not been established.

CONTRAINDICATIONS FELDENE should not be used in patients who have previously exhibited hypersensitivity to it, or in individuals with the syndrome comprised of bronchospasm, nasal polyps, and angioedema precipitated by aspirin or other nonsteroidal anti-inflammatory drugs.

WARNINGS Peptic ulceration, perforation, and G.I. bleeding—sometimes severe, and, in some instances fatal—have been reported with patients receiving FELDENE. If FELDENE must be given to patients with a history of upper gastrointestinal tract disease, the patient should be under close supervision (see ADVERSE REACTIONS). In controlled clinical trials, incidence of peptic ulceration with the maximum recommended FELDENE capsule dose of 20 mg per day was 0.8%. The use of doses higher than the recommended dose is associated with an increase in the incidence of gastrointestinal irritation and ulcers.

PRECAUTIONS As with other anti-inflammatory agents, long-term administration to animals results in renal papillary necrosis and related pathology in rats, mice, and dogs.

Acute renal failure and hyperkalemia as well as reversible elevations of BUN and serum creatinine have been reported with FELDENE. The effect is thought to result from inhibition of renal prostaglandin synthesis resulting in a change in medullary and deep cortical blood flow with an attendant effect on renal function. Patients with impaired renal function and on diuretics as well as elderly patients who have decreased renal function are more at risk. Because of the extensive renal excretion of piroxicam and its biotransformation products (less than 5% of the daily dose excreted unchanged, see CLINICAL PHARMACOLOGY), lower doses of piroxicam should be anticipated in patients with impaired renal function and they should be carefully monitored. In addition to reversible changes in renal function, interstitial nephritis, glomerulitis, papillary necrosis and the nephrotic syndrome have been reported with FELDENE.

Although other nonsteroidal anti-inflammatory drugs do not have the same direct effects on platelets that aspirin does, all drugs inhibiting prostaglandin biosynthesis do interfere with platelet function to some degree; therefore, patients who may be adversely affected by such an action should be carefully observed when FELDENE is administered.

Because of reports of adverse eye findings with nonsteroidal anti-inflammatory agents, it is recommended that patients who develop visual complaints during treatment with FELDENE have ophthalmic evaluation.

As with other nonsteroidal anti-inflammatory drugs, borderline elevations of one or more liver tests may occur in up to 15% of patients. These abnormalities may progress, may remain essentially unchanged, or may be transient with continued therapy. The SGPT (ALT) test is probably the most sensitive indicator of liver dysfunction. Meaningful (3 times the upper limit of normal) elevations of SGPT or SGOT (AST) occurred in controlled clinical trials in less than 1% of patients. A patient with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver test has occurred, should be evaluated for evidence of the development of more severe hepatic reaction while on therapy with FELDENE. Severe hepatic reactions, including jaundice and cases of fatal hepatitis, have been reported with FELDENE. Although such reactions are rare, if abnormal liver tests persist or worsen, if clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g. eosinophilia, rash, etc.), FELDENE should be discontinued. (See also ADVERSE REACTIONS.)

Although at the recommended dose of 20 mg/day of FELDENE increased fecal blood loss due to gastrointestinal irritation did not occur (see CLINICAL PHARMACOLOGY), in about 4% of the patients treated with FELDENE alone or concomitantly with aspirin, reductions in hemoglobin and hematocrit values were observed. Therefore, these values should be determined if signs or symptoms of anemia occur.

Peripheral edema has been observed in approximately 2% of the patients treated with FELDENE. Therefore, as with other nonsteroidal anti-inflammatory drugs, FELDENE should be used with caution in patients with heart failure, hypertension or other conditions predisposing to fluid retention, since its usage may be associated with a worsening of these conditions.

A combination of dermatological and/or allergic signs and symptoms suggestive of serum sickness have occasionally occurred in conjunction with the use of FELDENE. These include arthralgias, pruritus, fever, fatigue, and rash including vesiculo bullous reactions and exfoliative dermatitis.

DRUG INTERACTIONS FELDENE is highly protein bound, and, therefore, might be expected to displace other protein-bound drugs. Although this has not occurred in *in vitro* studies with coumarin-type anticoagulants, interactions with coumarin-type anticoagulants have been reported with FELDENE since marketing, therefore, physicians should closely monitor patients for a change in dosage requirements when administering FELDENE (piroxicam) to patients on coumarin-type anticoagulants and other highly protein-bound drugs.

Plasma levels of piroxicam are depressed to approximately 80% of their normal values when FELDENE (piroxicam) is administered in conjunction with aspirin (3900 mg/day), but concomitant administration of antacids has no effect on piroxicam plasma levels (see CLINICAL PHARMACOLOGY).

Nonsteroidal anti-inflammatory agents, including FELDENE, have been reported to increase steady state plasma lithium levels. It is recommended that plasma lithium levels be monitored when initiating, adjusting and discontinuing FELDENE.

Carcinogenesis, Chronic Animal Toxicity and Impairment of Fertility Subacute and chronic toxicity studies have been carried out in rats, mice, dogs, and monkeys.

The pathology most often seen was that characteristically associated with the animal toxicology of anti-inflammatory agents: renal papillary necrosis (see PRECAUTIONS) and gastrointestinal lesions.

In classical studies in laboratory animals piroxicam did not show any teratogenic potential.

Reproductive studies revealed no impairment of fertility in animals.

Pregnancy and Nursing Mothers Like other drugs which inhibit the synthesis and release of prostaglandins, piroxicam increased the incidence of dystocia and delayed parturition in pregnant animals when piroxicam administration was continued late into pregnancy. Gastrointestinal tract toxicity was increased in pregnant females in the last trimester of pregnancy compared to nonpregnant females or females in earlier trimesters of pregnancy.

FELDENE is not recommended for use in nursing mothers or in pregnant women because of the animal findings and since safety for such use has not been established in humans.

Use in Children Dosage recommendations and indications for use in children have not been established.

ADVERSE REACTIONS The incidence of adverse reactions to piroxicam is based on clinical trials involving approximately 2300 patients, about 400 of whom were treated for more than one year and 170 for more than two years. About 30% of all patients receiving daily doses of 20 mg of FELDENE experienced side effects. Gastrointestinal symptoms were the most prominent side effects—occurring in approximately 20% of the patients, which in most instances did not interfere with the course of therapy. Of the patients experiencing gastrointestinal side effects, approximately 5% discontinued therapy with an overall incidence of peptic ulceration of about 1%.

Other than the gastrointestinal symptoms, edema, dizziness, headache, changes in hematological parameters, and rash have been reported in a small percentage of patients. Routine ophthalmoscopy and slit-lamp examinations have revealed no evidence of ocular changes in 205 patients followed from 3 to 24 months while on therapy.

Incidence Greater Than 1% The following adverse reactions occurred more frequently than 1 in 100.

Gastrointestinal: stomatitis, anorexia, epigastric distress*, nausea*, constipation, abdominal discomfort, flatulence, diarrhea, abdominal pain, indigestion

Hematological: decreases in hemoglobin* and hematocrit* (see PRECAUTIONS), anemia, leucopenia, eosinophilia

Dermatologic: pruritus, rash

Central Nervous System: dizziness, somnolence, vertigo

Urogenital: BUN and creatinine elevations (see PRECAUTIONS)

Body as a Whole: headache, malaise

Special Senses: tinnitus

Cardiovascular/Respiratory: edema (see PRECAUTIONS)

*Reactions occurring in 3% to 9% of patients treated with FELDENE. Reactions occurring in 1-3% of patients are unmarked.

Incidence Less Than 1% (Causal Relationship Probable)

The following adverse reactions occurred less frequently than 1 in 100. The probability exists that there is a causal relationship between FELDENE and these reactions.

Gastrointestinal: liver function abnormalities, jaundice, hepatitis (see PRECAUTIONS), vomiting, hematemesis, melena, gastrointestinal bleeding, perforation and ulceration (see WARNINGS), dry mouth

Hematological: thrombocytopenia, petechial rash, ecchymosis, bone marrow depression including aplastic anemia, epistaxis

Dermatologic: sweating, erythema, bruising, desquamation, exfoliative dermatitis, erythema multiforme, toxic epidermal necrolysis, Stevens-Johnson syndrome, vesiculo bullous reaction, photoallergic skin reactions

Central Nervous System: depression, insomnia, nervousness

Urogenital: hematuria, proteinuria, interstitial nephritis, renal failure, hyperkalemia, glomerulitis, papillary necrosis, nephrotic syndrome (see PRECAUTIONS)

Body as a Whole: pain (colic), fever, flu-like syndrome (see PRECAUTIONS)

Special Senses: swollen eyes, blurred vision, eye irritations

Cardiovascular/Respiratory: hypertension, worsening of congestive heart failure (see PRECAUTIONS), exacerbation of angina

Metabolic: hypoglycemia, hyperglycemia, weight increase, weight decrease

Hypersensitivity: anaphylaxis, bronchospasm, urticaria/angioedema, vasculitis, "serum sickness" (see PRECAUTIONS)

Incidence Less Than 1% (Causal Relationship Unknown)

Other adverse reactions were reported with a frequency of less than 1 in 100, but a causal relationship between FELDENE and the reaction could not be determined.

Gastrointestinal: pancreatitis

Dermatologic: onycholysis, loss of hair

Central Nervous System: akathisia, hallucinations, mood alterations, dream abnormalities, mental confusion, paresthesias

Urogenital System: dysuria

Body as a Whole: weakness

Cardiovascular/Respiratory: palpitations, dyspnea

Hypersensitivity: positive ANA

OVERDOSAGE: In the event treatment for overdosage is required the long plasma half-life (see CLINICAL PHARMACOLOGY) of piroxicam should be considered. The absence of experience with acute overdosage precludes characterization of sequelae and recommendation of specific antidotal efficacy at this time. It is reasonable to assume, however, that the standard measures of gastric evacuation and general supportive therapy would apply. In addition to supportive measures, the use of activated charcoal may effectively reduce the absorption and reabsorption of piroxicam. Experiments in dogs have demonstrated that the use of multiple-dose treatments with activated charcoal could reduce the half-life of piroxicam elimination from 27 hours (without charcoal) to 11 hours and reduce the systemic bioavailability of piroxicam by as much as 37% when activated charcoal is given as late as 6 hours after administration of piroxicam.

ADMINISTRATION AND DOSAGE Rheumatoid Arthritis, Osteoarthritis It is recommended that FELDENE therapy be initiated and maintained at a single daily dose of 20 mg. If desired the daily dose may be divided. Because of the long half-life of FELDENE, steady-state blood levels are not reached for 7-12 days. Therefore although the therapeutic effects of FELDENE are evident early in treatment, there is a progressive increase in response over several weeks and the effect of therapy should not be assessed for two weeks.

Dosage recommendations and indications for use in children have not been established.

HOW SUPPLIED FELDENE Capsules for oral administration

Bottles of 100: 10 mg (NDC 0663-3220-66) maroon and blue #322
20 mg (NDC 0663-3230-66) maroon #323

Bottles of 500: 20 mg (NDC 0663-3230-73) maroon #323

Unit dose packages of 100: 20 mg (NDC 0663-3230-41) maroon #323

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Revised September 1984

FELDENE® 20 mg once-a-day for initiation and maintenance

Pfizer
LABORATORIES DIVISION
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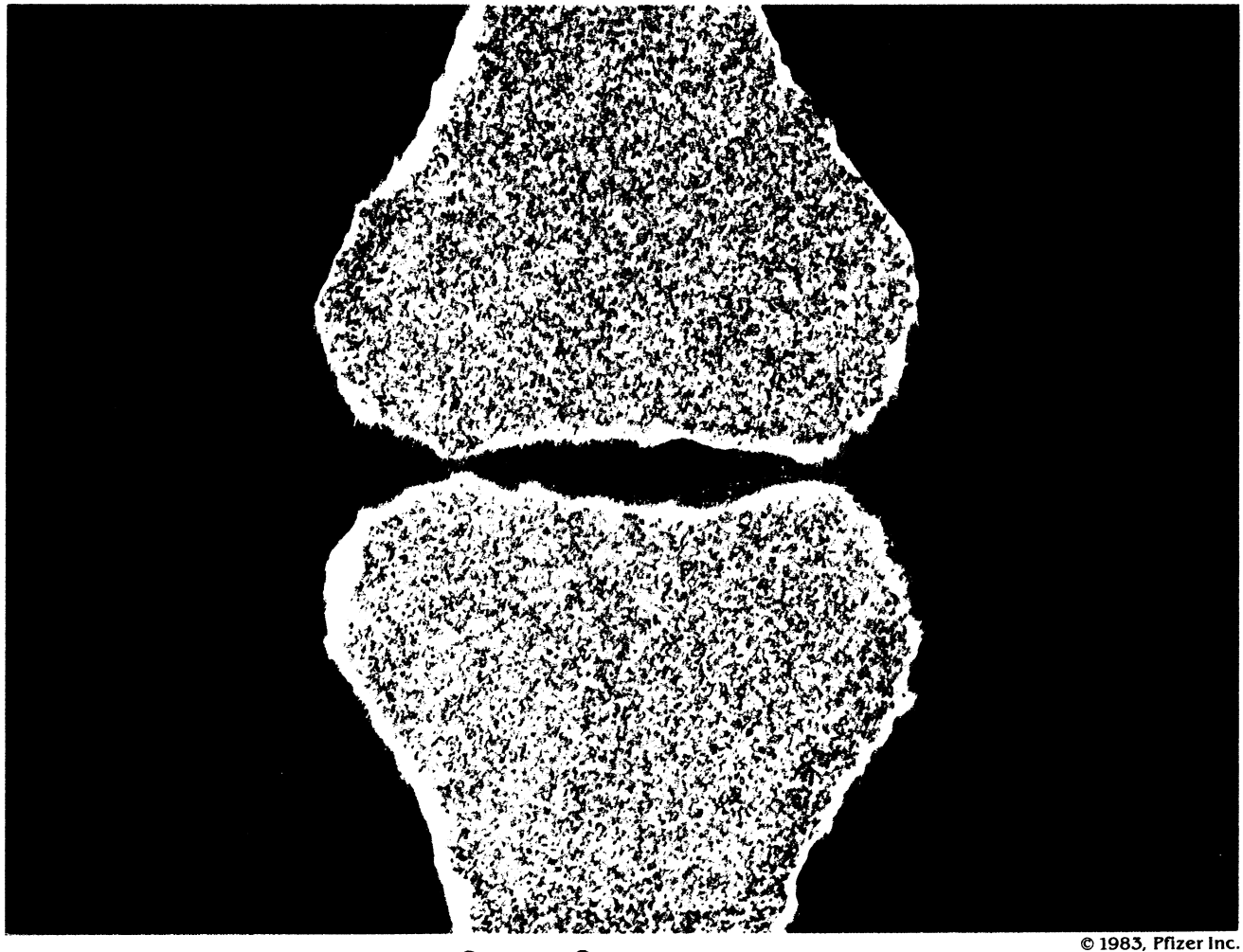

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You can help these patients feel better with one-a-day FELDENE (piroxicam).
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Feldene® *ONE-A-DAY*

(PIROXICAM) 20 mg capsules

Please see FELDENE (piroxicam) prescribing information on the following page.

Feldene®
(PIROXICAM) 20 mg capsules

Prescribing Information

FELDENE® (piroxicam) Capsules *For Oral Use*

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CLINICAL PHARMACOLOGY FELDENE has shown anti-inflammatory, analgesic and antipyretic properties in animals. Edema, erythema, tissue proliferation, fever, and pain can all be inhibited in laboratory animals by the administration of FELDENE. It is effective regardless of the etiology of the inflammation. The mode of action of FELDENE is not fully established at this time. However, a common mechanism for the above effects may exist in the ability of FELDENE to inhibit the biosynthesis of prostaglandins, known mediators of inflammation.

It is established that FELDENE does not act by stimulating the pituitary-adrenal axis.

FELDENE is well absorbed following oral administration. Drug plasma concentrations are proportional for 10 and 20 mg doses, generally peak within three to five hours after medication, and subsequently decline with a mean half-life of 50 hours (range of 30 to 86 hours, although values outside of this range have been encountered).

This prolonged half-life results in the maintenance of relatively stable plasma concentrations throughout the day on once daily doses and to significant drug accumulation upon multiple dosing. A single 20 mg dose generally produces peak piroxicam plasma levels of 1.5 to 2 mcg/ml, while maximum drug plasma concentrations, after repeated daily ingestion of 20 mg FELDENE, usually stabilize at 3-8 mcg/ml. Most patients approximate steady state plasma levels within 7 to 12 days. Higher levels, which approximate steady state at two to three weeks, have been observed in patients in whom longer plasma half-lives of piroxicam occurred.

FELDENE and its biotransformation products are excreted in urine and feces, with about twice as much appearing in the urine as the feces. Metabolism occurs by hydroxylation at the 5 position of the pyridyl side chain and conjugation of this product; by cyclodehydration; and by a sequence of reactions involving hydrolysis of the amide linkage, decarboxylation, ring contraction, and N-demethylation. Less than 5% of the daily dose is excreted unchanged.

Concurrent administration of aspirin (3900 mg/day) and FELDENE (20 mg/day), resulted in a reduction of plasma levels of piroxicam to about 80% of their normal values. The use of FELDENE in conjunction with aspirin is not recommended because data are inadequate to demonstrate that the combination produces greater improvement than that achieved with aspirin alone and the potential for adverse reactions is increased. Concomitant administration of antacids had no effect on FELDENE plasma levels. The effects of impaired renal function or hepatic disease on plasma levels have not been established.

FELDENE, like salicylates and other nonsteroidal anti-inflammatory agents, is associated with symptoms of gastrointestinal tract irritation (see ADVERSE REACTIONS). However, in a study utilizing ^{51}Cr-tagged red blood cells, 20 mg of FELDENE administered as a single dose for four days did not result in a significant increase in fecal blood loss and did not detectably affect the gastric mucosa. In the same study a total daily dose of 3900 mg of aspirin, i.e., 972 mg q.i.d., caused a significant increase in fecal blood loss and mucosal lesions as demonstrated by gastroscopy.

In controlled clinical trials, the effectiveness of FELDENE has been established for both acute exacerbations and long-term management of rheumatoid arthritis and osteoarthritis.

The therapeutic effects of FELDENE are evident early in the treatment of both diseases with a progressive increase in response over several (8-12) weeks. Efficacy is seen in terms of pain relief and, when present, subsidence of inflammation.

Doses of 20 mg/day FELDENE display a therapeutic effect comparable to therapeutic doses of aspirin, with a lower incidence of minor gastrointestinal effects and tinnitus.

FELDENE has been administered concomitantly with fixed doses of gold and corticosteroids. The existence of a "steroid-sparing" effect has not been adequately studied to date.

INDICATIONS AND USAGE FELDENE is indicated for acute or long-term use in the relief of signs and symptoms of the following:

1. osteoarthritis
2. rheumatoid arthritis

Dosage recommendations for use in children have not been established.

CONTRAINDICATIONS FELDENE should not be used in patients who have previously exhibited hypersensitivity to it, or in individuals with the syndrome comprised of bronchospasm, nasal polyps, and angioedema precipitated by aspirin or other nonsteroidal anti-inflammatory drugs.

WARNINGS Peptic ulceration, perforation, and G.I. bleeding—sometimes severe, and, in some instances fatal—have been reported with patients receiving FELDENE. If FELDENE must be given to patients with a history of upper gastrointestinal tract disease, the patient should be under close supervision (see ADVERSE REACTIONS). In controlled clinical trials, incidence of peptic ulceration with the maximum recommended FELDENE capsule dose of 20 mg per day was 0.8%. The use of doses higher than the recommended dose is associated with an increase in the incidence of gastrointestinal irritation and ulcers.

PRECAUTIONS As with other anti-inflammatory agents, long-term administration to animals results in renal papillary necrosis and related pathology in rats, mice, and dogs.

Acute renal failure and hyperkalemia as well as reversible elevations of BUN and serum creatinine have been reported with FELDENE. The effect is thought to result from inhibition of renal prostaglandin synthesis resulting in a change in medullary and deep cortical blood flow with an attendant effect on renal function. Patients with impaired renal function and on diuretics as well as elderly patients who have decreased renal function are more at risk. Because of the extensive renal excretion of piroxicam and its biotransformation products (less than 5% of the daily dose excreted unchanged, see CLINICAL PHARMACOLOGY), lower doses of piroxicam should be anticipated in patients with impaired renal function and they should be carefully monitored. In addition to reversible changes in renal function, interstitial nephritis, glomerulitis, papillary necrosis and the nephrotic syndrome have been reported with FELDENE.

Although other nonsteroidal anti-inflammatory drugs do not have the same direct effects on platelets that aspirin does, all drugs inhibiting prostaglandin biosynthesis do interfere with platelet function to some degree; therefore, patients who may be adversely affected by such an action should be carefully observed when FELDENE is administered.

Because of reports of adverse eye findings with nonsteroidal anti-inflammatory agents, it is recommended that patients who develop visual complaints during treatment with FELDENE have ophthalmic evaluation.

As with other nonsteroidal anti-inflammatory drugs, borderline elevations of one or more liver tests may occur in up to 15% of patients. These abnormalities may progress, may remain essentially unchanged, or may be transient with continued therapy. The SGPT (ALT) test is probably the most sensitive indicator of liver dysfunction. Meaningful (3 times the upper limit of normal) elevations of SGPT or SGOT (AST) occurred in controlled clinical trials in less than 1% of patients. A patient with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver test has occurred, should be evaluated for evidence of the development of more severe hepatic reaction while on therapy with FELDENE. Severe hepatic reactions, including jaundice and cases of fatal hepatitis, have been reported with FELDENE. Although such reactions are rare, if abnormal liver tests persist or worsen, if clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g. eosinophilia, rash, etc.), FELDENE should be discontinued. (See also ADVERSE REACTIONS.)

Although at the recommended dose of 20 mg/day of FELDENE increased fecal blood loss due to gastrointestinal irritation did not occur (see CLINICAL PHARMACOLOGY), in about 4% of the patients treated with FELDENE alone or concomitantly with aspirin, reductions in hemoglobin and hematocrit values were observed. Therefore, these values should be determined if signs or symptoms of anemia occur.

Peripheral edema has been observed in approximately 2% of the patients treated with FELDENE. Therefore, as with other nonsteroidal anti-inflammatory drugs, FELDENE should be used with caution in patients with heart failure, hypertension or other conditions predisposing to fluid retention, since its usage may be associated with a worsening of these conditions.

A combination of dermatological and/or allergic signs and symptoms suggestive of serum sickness have occasionally occurred in conjunction with the use of FELDENE. These include arthralgias, pruritus, fever, fatigue, and rash including vesiculo bullous reactions and exfoliative dermatitis.

DRUG INTERACTIONS FELDENE is highly protein bound, and, therefore, might be expected to displace other protein-bound drugs. Although this has not occurred in *in vitro* studies with coumarin-type anticoagulants, interactions with coumarin-type anticoagulants have been reported with FELDENE since marketing, therefore, physicians should closely monitor patients for a change in dosage requirements when administering FELDENE (piroxicam) to patients on coumarin-type anticoagulants and other highly protein-bound drugs.

20 mg once-a-day for initiation and maintenance

Plasma levels of piroxicam are depressed to approximately 80% of their normal values when FELDENE (piroxicam) is administered in conjunction with aspirin (3900 mg/day), but concomitant administration of antacids has no effect on piroxicam plasma levels (see CLINICAL PHARMACOLOGY).

Nonsteroidal anti-inflammatory agents, including FELDENE, have been reported to increase steady state plasma lithium levels. It is recommended that plasma lithium levels be monitored when initiating, adjusting and discontinuing FELDENE.

Carcinogenesis, Chronic Animal Toxicity and Impairment of Fertility Subacute and chronic toxicity studies have been carried out in rats, mice, dogs, and monkeys.

The pathology most often seen was that characteristically associated with the animal toxicology of anti-inflammatory agents: renal papillary necrosis (see PRECAUTIONS) and gastrointestinal lesions.

In classical studies in laboratory animals piroxicam did not show any teratogenic potential.

Reproductive studies revealed no impairment of fertility in animals.

Pregnancy and Nursing Mothers Like other drugs which inhibit the synthesis and release of prostaglandins, piroxicam increased the incidence of dystocia and delayed parturition in pregnant animals when piroxicam administration was continued late into pregnancy. Gastrointestinal tract toxicity was increased in pregnant females in the last trimester of pregnancy compared to nonpregnant females or females in earlier trimesters of pregnancy.

FELDENE is not recommended for use in nursing mothers or in pregnant women because of the animal findings and since safety for such use has not been established in humans.

Use in Children Dosage recommendations and indications for use in children have not been established.

ADVERSE REACTIONS The incidence of adverse reactions to piroxicam is based on clinical trials involving approximately 2300 patients, about 400 of whom were treated for more than one year and 170 for more than two years. About 30% of all patients receiving daily doses of 20 mg of FELDENE experienced side effects. Gastrointestinal symptoms were the most prominent side effects—occurring in approximately 20% of the patients, which in most instances did not interfere with the course of therapy. Of the patients experiencing gastrointestinal side effects, approximately 5% discontinued therapy with an overall incidence of peptic ulceration of about 1%.

Other than the gastrointestinal symptoms, edema, dizziness, headache, changes in hematological parameters, and rash have been reported in a small percentage of patients. Routine ophthalmoscopy and slit-lamp examinations have revealed no evidence of ocular changes in 205 patients followed from 3 to 24 months while on therapy.

Incidence Greater Than 1% The following adverse reactions occurred more frequently than 1 in 100.

Gastrointestinal: stomatitis, anorexia, epigastric distress*, nausea*, constipation, abdominal discomfort, flatulence, diarrhea, abdominal pain, indigestion

Hematological: decreases in hemoglobin* and hematocrit* (see PRECAUTIONS), anemia, leucopenia, eosinophilia

Dermatologic: pruritus, rash

Central Nervous System: dizziness, somnolence, vertigo

Urogenital: BUN and creatinine elevations (see PRECAUTIONS)

Body as a Whole: headache, malaise

Special Senses: tinnitus

Cardiovascular/Respiratory: edema (see PRECAUTIONS)

*Reactions occurring in 3% to 9% of patients treated with FELDENE. Reactions occurring in 1-3% of patients are unmarked.

Incidence Less Than 1% (Causal Relationship Probable)

The following adverse reactions occurred less frequently than 1 in 100. The probability exists that there is a causal relationship between FELDENE and these reactions.

Gastrointestinal: liver function abnormalities, jaundice, hepatitis (see PRECAUTIONS), vomiting, hematemesis, melena, gastrointestinal bleeding, perforation and ulceration (see WARNINGS), dry mouth

Hematological: thrombocytopenia, petechial rash, ecchymosis, bone marrow depression including aplastic anemia, epistaxis

Dermatologic: sweating, erythema, bruising, desquamation, exfoliative dermatitis, erythema multiforme, toxic epidermal necrolysis, Stevens-Johnson syndrome, vesiculo bullous reaction, photoallergic skin reactions

Central Nervous System: depression, insomnia, nervousness

Urogenital: hematuria, proteinuria, interstitial nephritis, renal failure, hyperkalemia, glomerulitis, papillary necrosis, nephrotic syndrome (see PRECAUTIONS)

Body as a Whole: pain (colic), fever, flu-like syndrome (see PRECAUTIONS)

Special Senses: swollen eyes, blurred vision, eye irritations

Cardiovascular/Respiratory: hypertension, worsening of congestive heart failure (see PRECAUTIONS), exacerbation of angina

Metabolic: hypoglycemia, hyperglycemia, weight increase, weight decrease

Hypersensitivity: anaphylaxis, bronchospasm, urticaria/angioedema, vasculitis, "serum sickness" (see PRECAUTIONS)

Incidence Less Than 1% (Causal Relationship Unknown)

Other adverse reactions were reported with a frequency of less than 1 in 100, but a causal relationship between FELDENE and the reaction could not be determined.

Gastrointestinal: pancreatitis

Dermatologic: onycholysis, loss of hair

Central Nervous System: akathisia, hallucinations, mood alterations, dream abnormalities, mental confusion, paresthesias

Urogenital System: dysuria

Body as a Whole: weakness

Cardiovascular/Respiratory: palpitations, dyspnea

Hypersensitivity: positive ANA

OVERDOSAGE: In the event treatment for overdosage is required the long plasma half-life (see CLINICAL PHARMACOLOGY) of piroxicam should be considered. The absence of experience with acute overdosage precludes characterization of sequelae and recommendation of specific antidotal efficacy at this time. It is reasonable to assume, however, that the standard measures of gastric evacuation and general supportive therapy would apply. In addition to supportive measures, the use of activated charcoal may effectively reduce the absorption and reabsorption of piroxicam. Experiments in dogs have demonstrated that the use of multiple-dose treatments with activated charcoal could reduce the half-life of piroxicam elimination from 27 hours (without charcoal) to 11 hours and reduce the systemic bioavailability of piroxicam by as much as 37% when activated charcoal is given as late as 6 hours after administration of piroxicam.

ADMINISTRATION AND DOSAGE Rheumatoid Arthritis, Osteoarthritis It is recommended that FELDENE therapy be initiated and maintained at a single daily dose of 20 mg. If desired the daily dose may be divided. Because of the long half-life of FELDENE, steady-state blood levels are not reached for 7-12 days. Therefore although the therapeutic effects of FELDENE are evident early in treatment, there is a progressive increase in response over several weeks and the effect of therapy should not be assessed for two weeks.

Dosage recommendations and indications for use in children have not been established.

HOW SUPPLIED FELDENE Capsules for oral administration

Bottles of 100: 10 mg (NDC 0663-3220-66) maroon and blue #322
20 mg (NDC 0663-3230-66) maroon #323

Bottles of 500: 20 mg (NDC 0663-3230-73) maroon #323

Unit dose packages of 100: 20 mg (NDC 0663-3230-41) maroon #323

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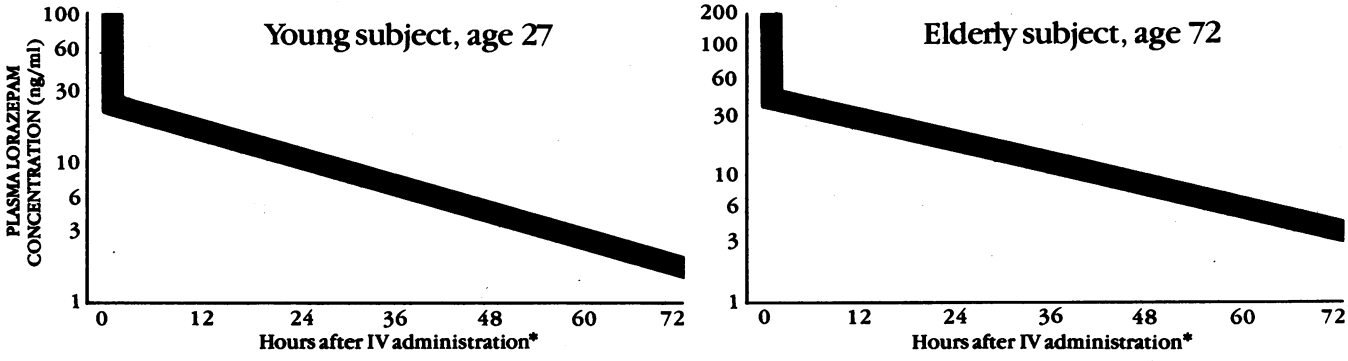
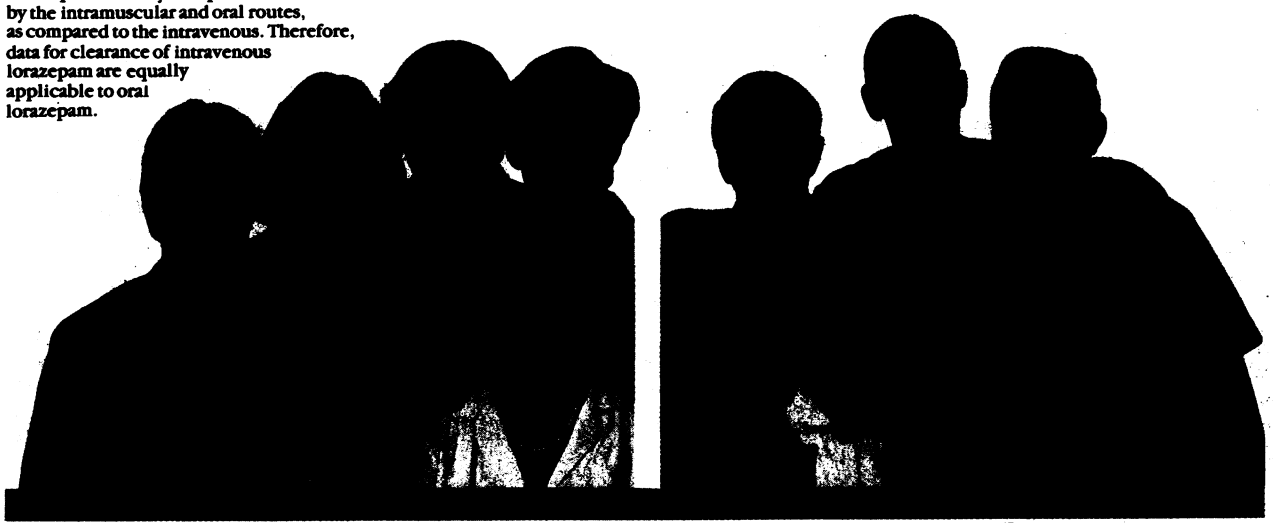
Among leading benzodiazepines, only Ativan has proof... pharmacokinetics not significantly altered by age.[1]

Representative charts of comparison testing



Lorazepam is nearly 100 percent bioavailable by the intramuscular and oral routes, as compared to the intravenous. Therefore, data for clearance of intravenous lorazepam are equally applicable to oral lorazepam.



- **Clearance not significantly delayed by age, liver or kidney dysfunction**
- **Cumulative sedative effects seldom a problem**
- **Available in 0.5-mg tablets to facilitate the recommended geriatric starting dosage**

1. Greenblatt DJ: Clinical study, pharmacokinetics and bioavailability in the elderly, Ativan® (lorazepam). Data on file, Wyeth Laboratories.

*Fourteen subjects, aged 60 to 84 years, participated in the study. Twelve subjects, aged 19 to 32 years, served as "young controls." Subject dosage was adjusted for body weight and ranged from 1.5 mg to 3.0 mg of lorazepam. Within the study, lorazepam clearance was monitored following IV, IM and oral administration in the elderly group and following IV administration in the control group. The effect of aging on total clearance of lorazepam was relatively small and not statistically significant. Half-life values following the three different routes of administration were essentially identical.

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For further information about Charter Baywood or admission procedures, contact:

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Hospital Administrator: Diana Goulet

Charter Grove Hospital

2005 Kellogg Drive
Corona, California 91720
(714) 735-2910

Beds: 86
Psychiatric Staff: 15
Programs: Adult and Adolescent Psychiatric; Adult Addictive Disease.

Other Programs: Women's Program; Eating Disorders; and Christian Psychiatric

For further information about Charter Grove or admission procedures, contact:

Medical Director: William Cohen, M.D.
Hospital Administrator: Jim Fridlington

Charter Oak Hospital

1161 East Covina Blvd.
Covina, California 91724
(213) 966-1632

Beds: 74
Psychiatric Staff: 14
Programs: Adult, Adolescent and Child Psychiatric; Adult Addictive Disease

Other Programs: Premenstrual Syndrome Clinic

For further information about Charter Oak or admission procedures, contact:

President of Medical Staff:
Adib Bitar, M.D.
Hospital Administrator: Jim Sholes

Charter Pacific Hospital

4025 West 226th St.
Torrance, California 90505
(213) 373-7733

Beds: 96
Psychiatric Staff: 36
Programs: Adolescent, Child and Young Adult Psychiatric; Adult and Adolescent Addictive Disease

Other Programs: Pediatric Neuro/Development Diagnostic Unit; Charter Clinic, in Santa Ana, offers Neuropsychological child and adolescent services.

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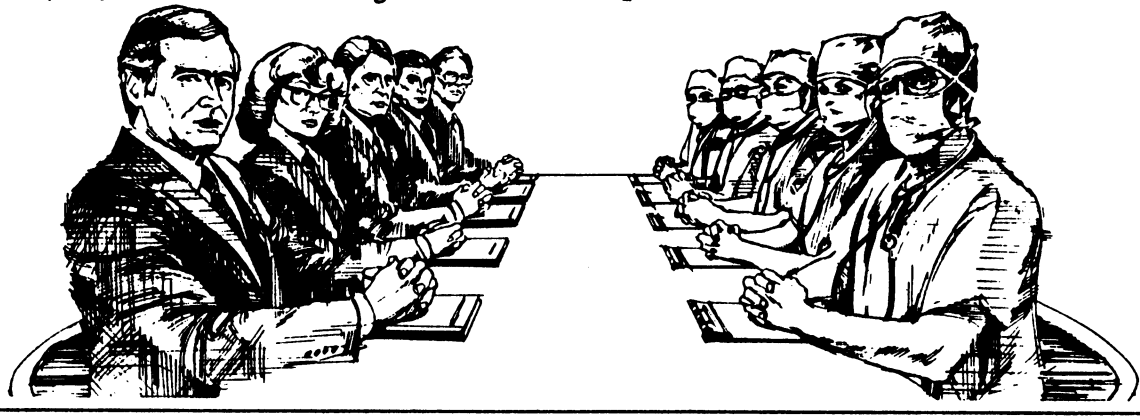

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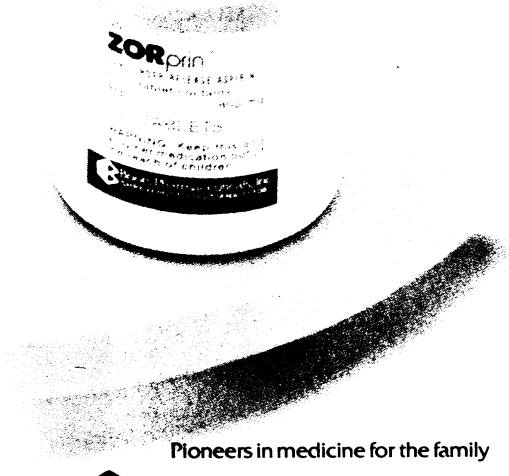

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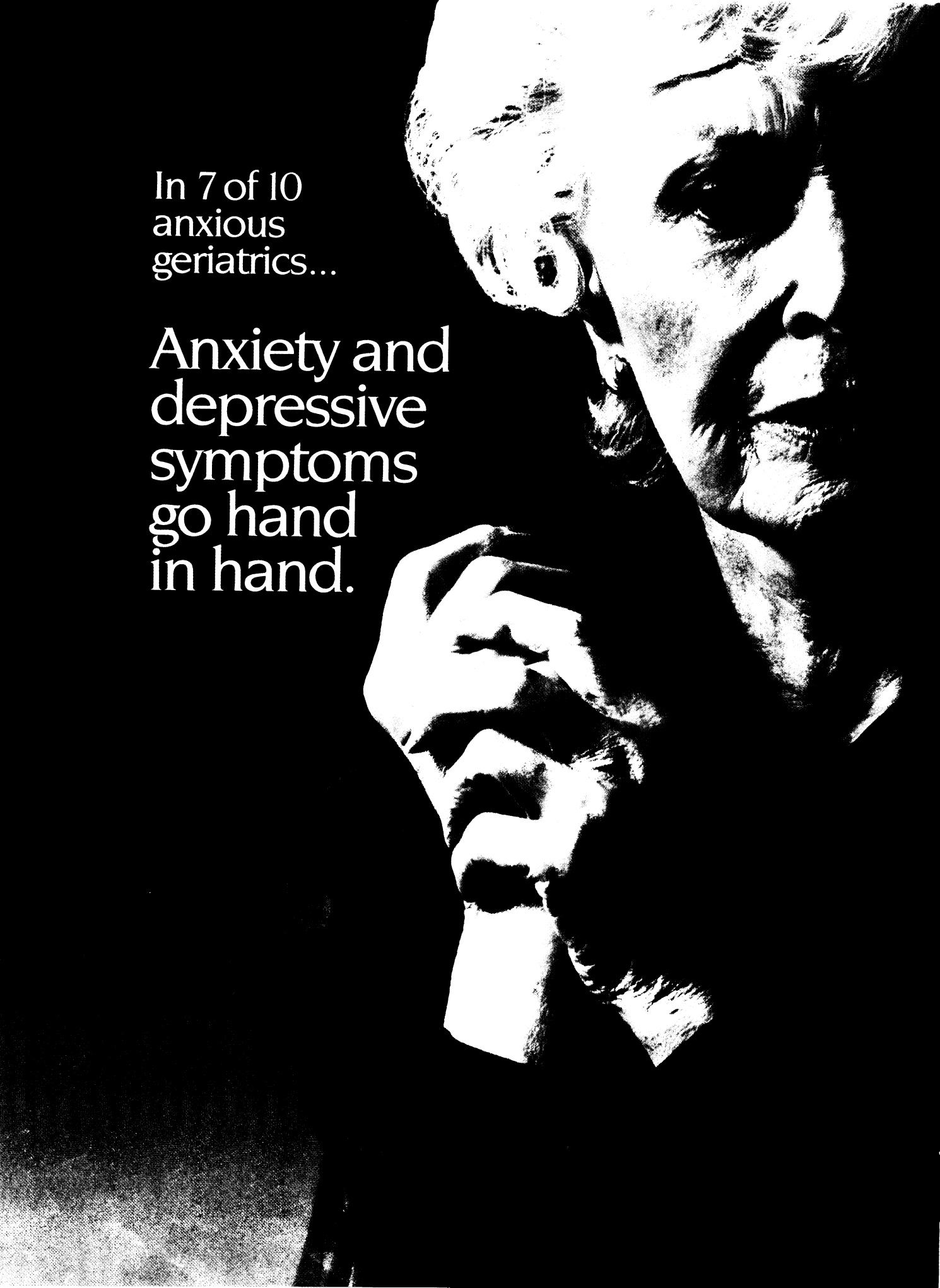
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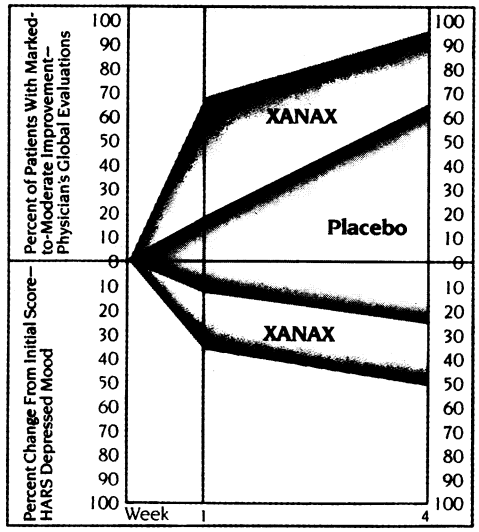

In a recent clinical study[1] of 83 geriatric patients with clinical anxiety, 73% were diagnosed as having symptoms of depressed mood.

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1. Cohn JB: Double-blind safety and efficacy comparison of alprazolam and placebo in the treatment of anxiety in geriatric patients. *Curr Ther Res* 1984;35(1):100-112.

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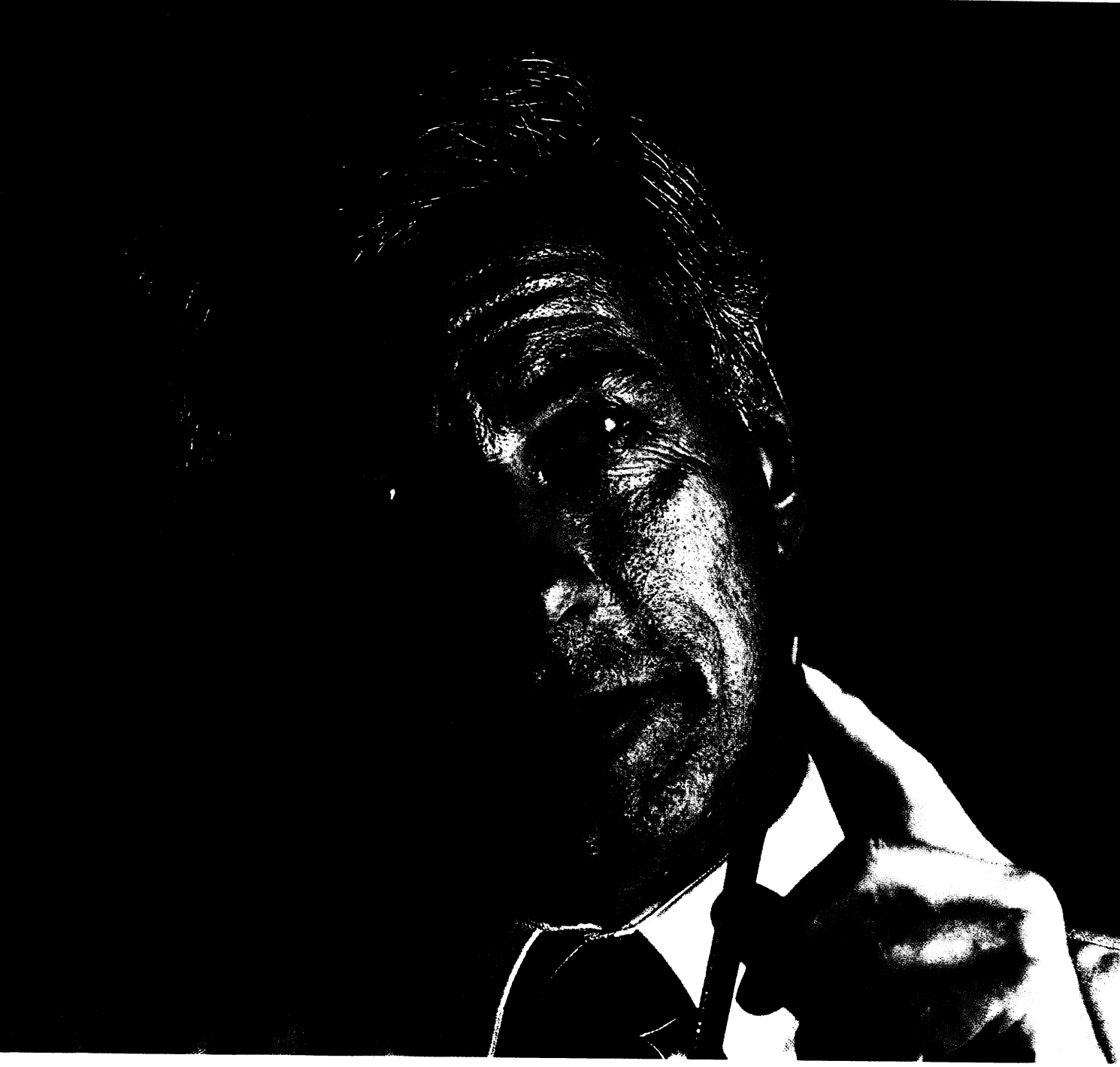

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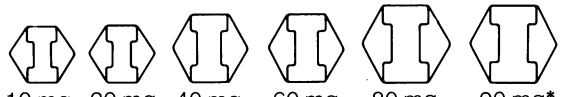
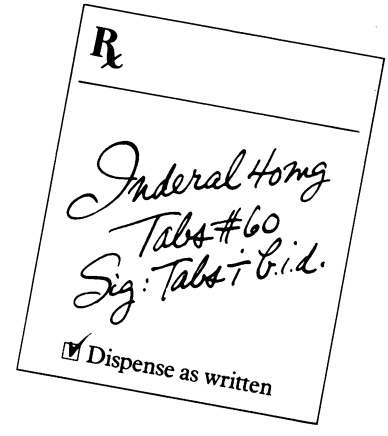


10 mg 20 mg 40 mg 60 mg 80 mg 90 mg*



BRIEF SUMMARY (FOR FULL PRESCRIBING INFORMATION, SEE PACKAGE CIRCULAR.)

INDERAL® (propranolol hydrochloride) Tablets

CONTRAINDICATIONS

INDERAL is contraindicated in 1) cardiogenic shock, 2) sinus bradycardia and greater than first degree block, 3) bronchial asthma, 4) congestive heart failure (see WARNINGS) unless the failure is secondary to a tachyarrhythmia treatable with INDERAL.

WARNINGS

CARDIAC FAILURE: Sympathetic stimulation may be a vital component supporting circulatory function in patients with congestive heart failure, and its inhibition by beta blockade may precipitate more severe failure. Although beta blockers should be avoided in overt congestive heart failure, if necessary they can be used with close follow-up in patients with a history of failure who are well compensated and are receiving digitalis and diuretics. Beta-adrenergic blocking agents do not abolish the inotropic action of digitalis on heart muscle.

IN PATIENTS WITHOUT A HISTORY OF HEART FAILURE, continued use of beta blockers can, in some cases, lead to cardiac failure. Therefore, at the first sign or symptom of heart failure, the patient should be digitalized and/or treated with diuretics, and the response observed closely, or INDERAL should be discontinued (gradually, if possible).

IN PATIENTS WITH ANGINA PECTORIS, there have been reports of exacerbation of angina and, in some cases, myocardial infarction, following abrupt discontinuance of INDERAL therapy. Therefore, when discontinuance of INDERAL is planned the dosage should be gradually reduced over at least a few weeks and the patient should be cautioned against interruption or cessation of therapy without the physician's advice. If INDERAL therapy is interrupted and exacerbation of angina occurs, it usually is advisable to reinstitute INDERAL therapy and take other measures appropriate for the management of unstable angina pectoris. Since coronary artery disease may be unrecognized, it may be prudent to follow the above advice in patients considered at risk of having occult atherosclerotic heart disease who are given propranolol for other indications.

Nonallergic Bronchospasm (e.g., chronic bronchitis, emphysema)—PATIENTS WITH BRONCHOSPASTIC DISEASES SHOULD IN GENERAL NOT RECEIVE BETA BLOCKERS. INDERAL should be administered with caution since it may block bronchodilation produced by endogenous and exogenous catecholamine stimulation of beta receptors.

MAJOR SURGERY: The necessity or desirability of withdrawal of beta-blocking therapy prior to major surgery is controversial. It should be noted, however, that the impaired ability of the heart to respond to reflex adrenergic stimuli may augment the risks of general anesthesia and surgical procedures.

INDERAL, like other beta blockers, is a competitive inhibitor of beta-receptor agonists and its effects can be reversed by administration of such agents, e.g., dobutamine or isoproterenol. However, such patients may be subject to protracted severe hypotension. Difficulty in starting and maintaining the heartbeat has also been reported with beta blockers.

DIABETES AND HYPOGLYCEMIA: Beta-adrenergic blockade may prevent the appearance of certain premonitory signs and symptoms (pulse rate and pressure changes) of acute hypoglycemia in labile insulin-dependent diabetes. In these patients, it may be more difficult to adjust the dosage of insulin.

THYROTOXICOSIS: Beta blockade may mask certain clinical signs of hyperthyroidism. Therefore, abrupt withdrawal of propranolol may be followed by an exacerbation of symptoms of hyperthyroidism, including thyroid storm. Propranolol does not distort thyroid function tests.

IN PATIENTS WITH WOLFF-PARKINSON-WHITE SYNDROME, several cases have been reported in which, after propranolol, the tachycardia was replaced by a severe bradycardia requiring a demand pacemaker. In one case this resulted after an initial dose of 5 mg propranolol.

PRECAUTIONS

General: Propranolol should be used with caution in patients with impaired hepatic or renal function. INDERAL is not indicated for the treatment of hypertensive emergencies.

Beta-adrenoreceptor blockade can cause reduction of intraocular pressure. Patients should be told that INDERAL (propranolol hydrochloride) may interfere with the glaucoma screening test. Withdrawal may lead to a return of increased intraocular pressure.

Clinical Laboratory Tests: Elevated blood urea levels in patients with severe heart disease, elevated serum transaminase, alkaline phosphatase, lactate dehydrogenase.

DRUG INTERACTIONS: Patients receiving catecholamine-depleting drugs such as reserpine should be closely observed if INDERAL is administered. The added catecholamine-blocking action may produce an excessive reduction of resting sympathetic nervous activity which may result in hypotension, marked bradycardia, vertigo, syncopal attacks, or orthostatic hypotension.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term studies in animals have been conducted to evaluate toxic effects and carcinogenic potential. In 18-month studies in both rats and mice, employing doses up to 150 mg/kg/day, there was no evidence of significant drug-induced toxicity. There were no drug-related tumorigenic effects at any of the dosage levels. Reproductive studies in animals did not show any impairment of fertility that was attributable to the drug.

Pregnancy: Pregnancy Category C. INDERAL has been shown to be embryotoxic in animal studies at doses about 10 times greater than the maximum recommended human dose.

There are no adequate and well-controlled studies in pregnant women. INDERAL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: INDERAL is excreted in human milk. Caution should be exercised when INDERAL is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Most adverse effects have been mild and transient and have rarely required the withdrawal of therapy.

Cardiovascular: bradycardia; congestive heart failure; intensification of AV block; hypotension; paresthesia of hands; thrombocytopenic purpura; arterial insufficiency, usually of the Raynaud type.

Central Nervous System: Lightheadedness; mental depression manifested by insomnia, lassitude, weakness, fatigue; reversible mental depression progressing to catatonia; visual disturbances; hallucinations; an acute reversible syndrome characterized by disorientation for time and place, short-term memory loss, emotional lability, slightly clouded sensorium, and decreased performance on neuropsychometrics.

Gastrointestinal: nausea, vomiting, epigastric distress, abdominal cramping, diarrhea, constipation, mesenteric arterial thrombosis, ischemic colitis.

Allergic: pharyngitis and agranulocytosis, erythematous rash, fever combined with aching and sore throat, laryngospasm and respiratory distress.

Respiratory: bronchospasm.

Hematologic: agranulocytosis, nonthrombocytopenic purpura, thrombocytopenic purpura.

Auto-Immune: In extremely rare instances, systemic lupus erythematosus has been reported.

Miscellaneous: alopecia, LE-like reactions, psoriasiform rashes, dry eyes, male impotence, and Peyronie's disease have been reported rarely. Oculomucocutaneous reactions involving the skin, serous membranes and conjunctivae reported for a beta blocker (practolol) have not been associated with propranolol.

*The appearance of INDERAL tablets is a registered trademark of Ayerst Laboratories.

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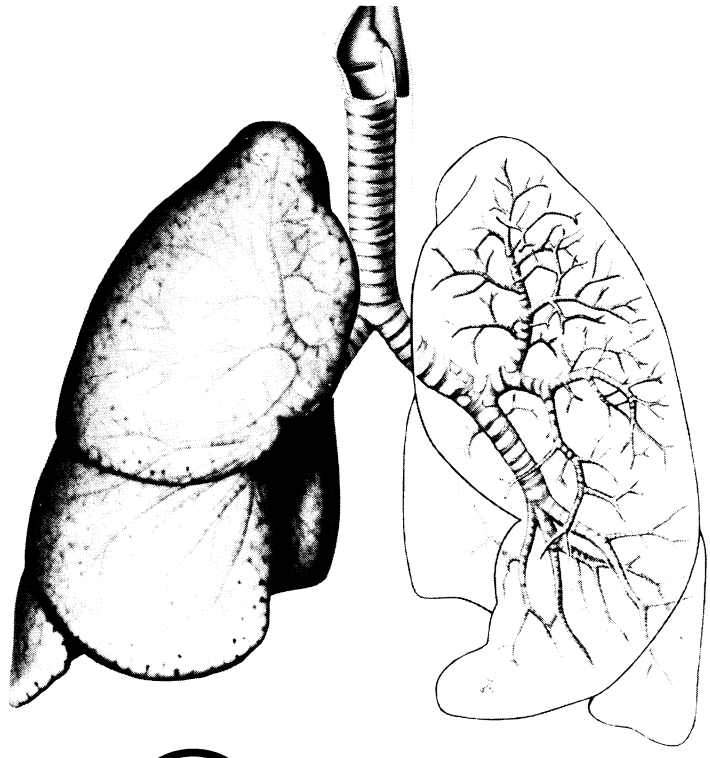
New York, N.Y. 10017

Consider the causative organisms...



Ceclor®
cefaclor
250-mg Pulvules® t.i.d.

offers effectiveness against the major causes of bacterial bronchitis

H. influenzae, H. influenzae, S. pneumoniae, S. pyogenes
(ampicillin-susceptible) (ampicillin-resistant)

Brief Summary. Consult the package literature for prescribing information.

Indications and Usage: Ceclor* (cefaclor, Lilly) is indicated in the treatment of the following infections when caused by susceptible strains of the designated microorganisms:

Lower respiratory infections, including pneumonia caused by *Streptococcus pneumoniae (Diplococcus pneumoniae), Haemophilus influenzae*, and *S. pyogenes* (group A beta-hemolytic streptococci).

Appropriate culture and susceptibility studies should be performed to determine susceptibility of the causative organism to Ceclor.

Contraindication: Ceclor is contraindicated in patients with known allergy to the cephalosporin group of antibiotics.

Warnings: IN PENICILLIN-SENSITIVE PATIENTS, CEPHALOSPORIN ANTIBIOTICS SHOULD BE ADMINISTERED CAUTIOUSLY. THERE IS CLINICAL AND LABORATORY EVIDENCE OF PARTIAL CROSS-ALLERGENICITY OF THE PENICILLINS AND THE CEPHALOSPORINS, AND THERE ARE INSTANCES IN WHICH PATIENTS HAVE HAD REACTIONS, INCLUDING ANAPHYLAXIS, TO BOTH DRUG CLASSES.

Antibiotics, including Ceclor, should be administered cautiously to any patient who has demonstrated some form of allergy, particularly to drugs.

Pseudomembranous colitis has been reported with virtually all broad-spectrum antibiotics (including macrolides, semisynthetic penicillins, and cephalosporins); therefore, it is important to consider its diagnosis in patients who develop diarrhea in association with the use of antibiotics. Such colitis may range in severity from mild to life-threatening.

Treatment with broad-spectrum antibiotics alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is one primary cause of antibiotic-associated colitis.

Mild cases of pseudomembranous colitis usually respond to drug discontinuance alone. In moderate to severe cases, management should include sigmoidoscopy, appropriate bacteriologic studies, and fluid, electrolyte, and protein supplementation. When the colitis does not improve after the drug has been discontinued, or when it is severe, oral vancomycin is the drug of choice for antibiotic-associated pseudomembranous colitis produced by *C. difficile*. Other causes of colitis should be ruled out.

Precautions: *General Precautions* — If an allergic reaction to Ceclor* (cefaclor, Lilly) occurs, the drug should be discontinued, and, if necessary, the patient should be treated with appropriate agents, e.g., pressor amines, antihistamines, or corticosteroids.

Prolonged use of Ceclor may result in the overgrowth of nonsusceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Positive direct Coombs' tests have been reported during treatment with the cephalosporin antibiotics. In hematologic studies or in transfusion cross-matching procedures when antiglobulin tests are performed on the minor side or in Coombs' testing of newborns whose mothers have received cephalosporin antibiotics before parturition, it should be recognized that a positive Coombs' test may be due to the drug.

Ceclor should be administered with caution in the presence of markedly impaired renal function. Under such conditions, careful clinical observation and laboratory studies should be made, because safe dosage may be lower than that usually recommended.

As a result of administration of Ceclor, a false-positive reaction for glucose in the urine may occur. This has been observed with Benedict's and Fehling's solutions and also with Clinitest* tablets but not with Tes-Tape* (Glucose Enzymatic Test Strip, USP, Lilly).

Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

Usage in Pregnancy — Pregnancy Category B — Reproduction studies have been performed in mice and rats at doses up to 12 times the human dose and in ferrets given three times the maximum human dose and have revealed no evidence of impaired fertility or harm to the fetus due to Ceclor* (cefaclor, Lilly). There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers — Small amounts of Ceclor have been detected in mother's milk following administration of single 500-mg doses. Average levels were 0.18, 0.20, 0.21, and 0.16 mcg/ml at two, three, four, and five hours respectively. Trace amounts were detected at one hour. The effect on nursing infants is not known. Caution should be exercised when Ceclor is administered to a nursing woman.

Usage in Children — Safety and effectiveness of this product for use in infants less than one month of age have not been established.

Adverse Reactions: Adverse effects considered related to therapy with Ceclor are uncommon and are listed below.

Gastrointestinal symptoms occur in about 2.5 percent of patients and include diarrhea (1 in 70).

Symptoms of pseudomembranous colitis may appear either during or after antibiotic treatment. Nausea and vomiting have been reported rarely.

Hypersensitivity reactions have been reported in about 1.5 percent of patients and include morbilliform eruptions (1 in 100). Pruritus, urticaria, and positive Coombs' tests each occur in less than 1 in 200 patients. Cases of serum-sickness-like reactions (erythema multiforme or the above skin manifestations accompanied by arthritis/arthralgia and, frequently, fever) have been reported. These reactions are apparently due to hypersensitivity and have usually occurred during or following a second course of therapy with Ceclor. Such reactions have been reported more frequently in children than in adults. Signs and symptoms usually occur a few days after initiation of therapy and subside within a few days after cessation of therapy. No serious sequelae have been reported. Antihistamines and corticosteroids appear to enhance resolution of the syndrome.

Cases of anaphylaxis have been reported, half of which have occurred in patients with a history of penicillin allergy.

Other effects considered related to therapy included eosinophilia (1 in 50 patients) and genital pruritus or vaginitis (less than 1 in 100 patients).

Causal Relationship Uncertain — Transitory abnormalities in clinical laboratory test results have been reported. Although they were of uncertain etiology, they are listed below to serve as alerting information for the physician.

Hepatic — Slight elevations in SGOT, SGPT, or alkaline phosphatase values (1 in 40).

Hematopoietic — Transient fluctuations in leukocyte count, predominantly lymphocytosis occurring in infants and young children (1 in 40).

Renal — Slight elevations in BUN or serum creatinine (less than 1 in 500) or abnormal urinalysis (less than 1 in 200).

[061782R]

Note: Ceclor* (cefaclor, Lilly) is contraindicated in patients with known allergy to the cephalosporins and should be given cautiously to penicillin-allergic patients.

Penicillin is the usual drug of choice in the treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever. See prescribing information.

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Additional information available to the profession on request from Eli Lilly and Company, Indianapolis, Indiana 46285

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Carolina, Puerto Rico 00630

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Arthritis pain after 50

Age is no barrier to the benefits of Motrin 600 mg tablets

The pain-relieving power of *Motrin* 600 mg tablets is welcome at any age. The advantages of *Motrin* become more important as patients grow older.

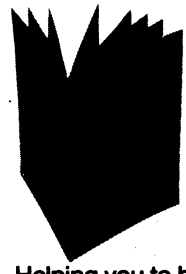
Advanced age has little or no influence on the pharmacokinetics of *Motrin.*

Motrin is as effective as indomethacin in relieving arthritis pain and inflammation. *Motrin* causes significantly fewer CNS effects and about half as many GI complaints as indomethacin.

Motrin relieves pain as effectively as a combination of aspirin 650 mg plus codeine 60 mg, as documented in analgesia studies.

Motrin has no significant effect on clotting factors in patients on coumarin-type anticoagulants in controlled studies. *Motrin* should be used with caution in persons with intrinsic coagulation defects and in those on anticoagulant therapy.

Motrin is rapidly metabolized and does not accumulate. *Motrin* provides better control of therapy, rapid response to dosage adjustment, and permits tailoring dosage to each patient's needs.



New: The Motrin Patient Brochure
An easy-to-read booklet, provided to physicians, that helps patients understand their arthritis therapy... encourages their cooperation.

Helping you to help your patients—
Ask your Upjohn Representative for a complimentary supply.

The confidence that comes from experience...good reason to prescribe

Motrin® 600 mg TABLETS (ibuprofen)

One tablet t.i.d.

Please turn page for a brief summary of prescribing information.

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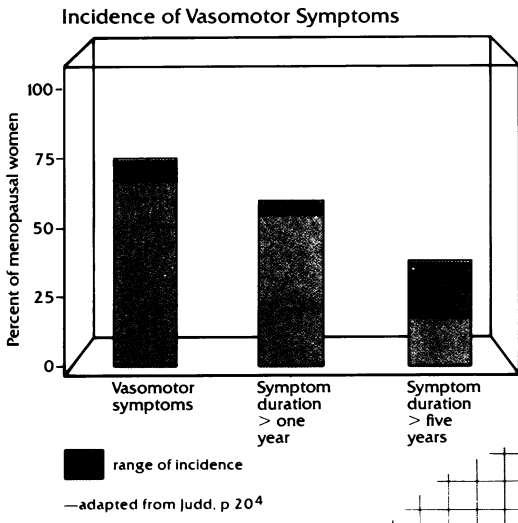
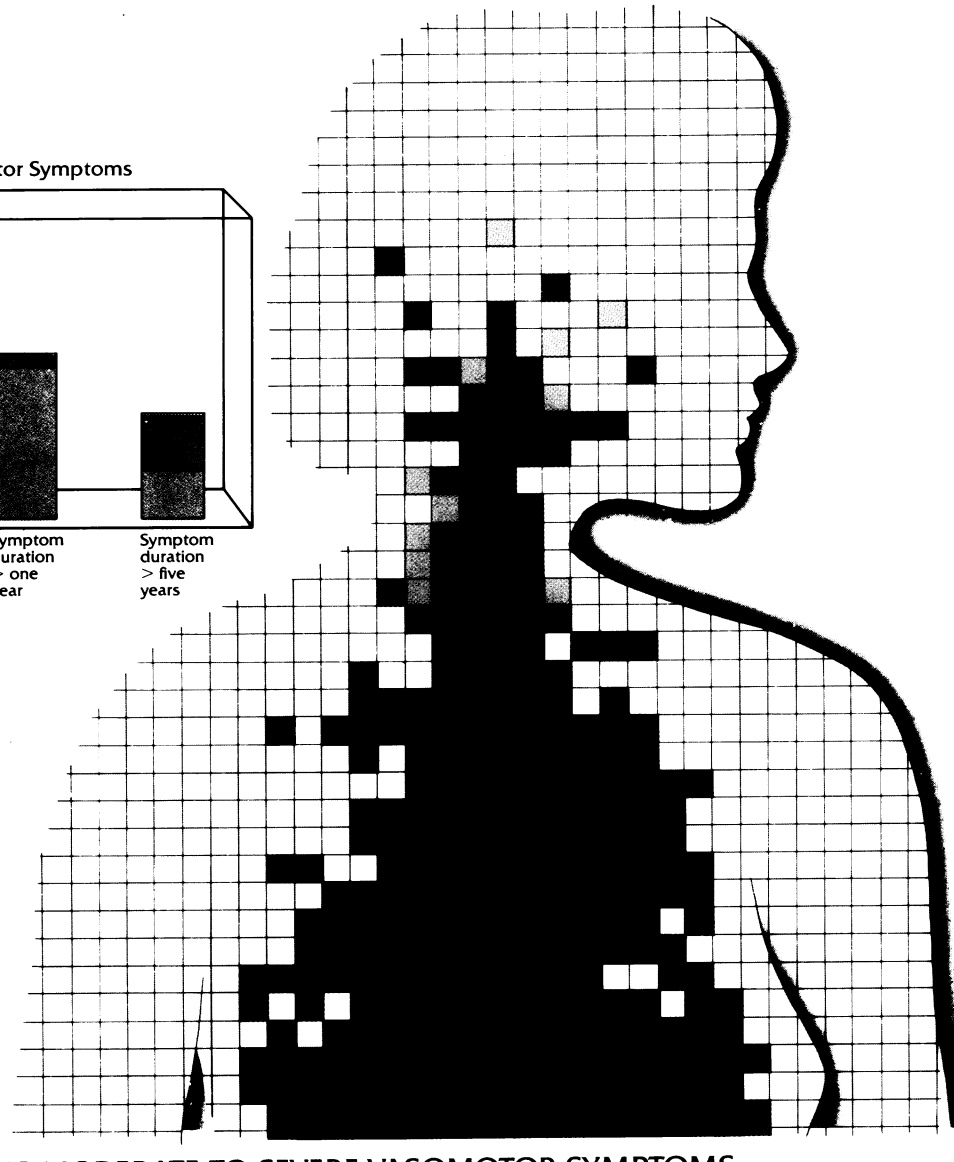
A GREAT WAY TO SERVE

1058

VASOMOTOR SYMPTOMS THAT DEMAND INTERVENTION





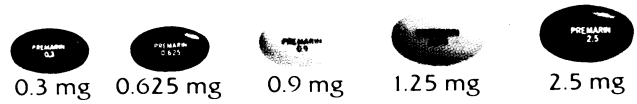
PREMARIN RELIEVES MODERATE TO SEVERE VASOMOTOR SYMPTOMS

Vasomotor symptoms are the most common manifestation of the menopause, affecting up to 75% of menopausal women. Of these, 80% may suffer for more than a year and up to 50% for more than five years.[4] These symptoms can disrupt a woman's life by chronically interrupting sleep, resulting in anxiety and irritability.

In a study of postmenopausal women suffering severe episodes of cutaneous flushing, symptoms improved markedly after administration of estrogen[5]—the treatment of choice for moderate to severe vasomotor symptoms.[6] The estrogen of choice is PREMARIN, the most widely prescribed estrogen for over 40 years. PREMARIN (Conjugated Estrogens Tablets, U.S.P.) relieves moderate to severe vasomotor symptoms of the natural menopause, as well as the acute and often severe symptoms of surgical menopause.

PREMARIN®

(CONJUGATED ESTROGENS TABLETS, U.S.P.)



0.3 mg 0.625 mg 0.9 mg 1.25 mg 2.5 mg

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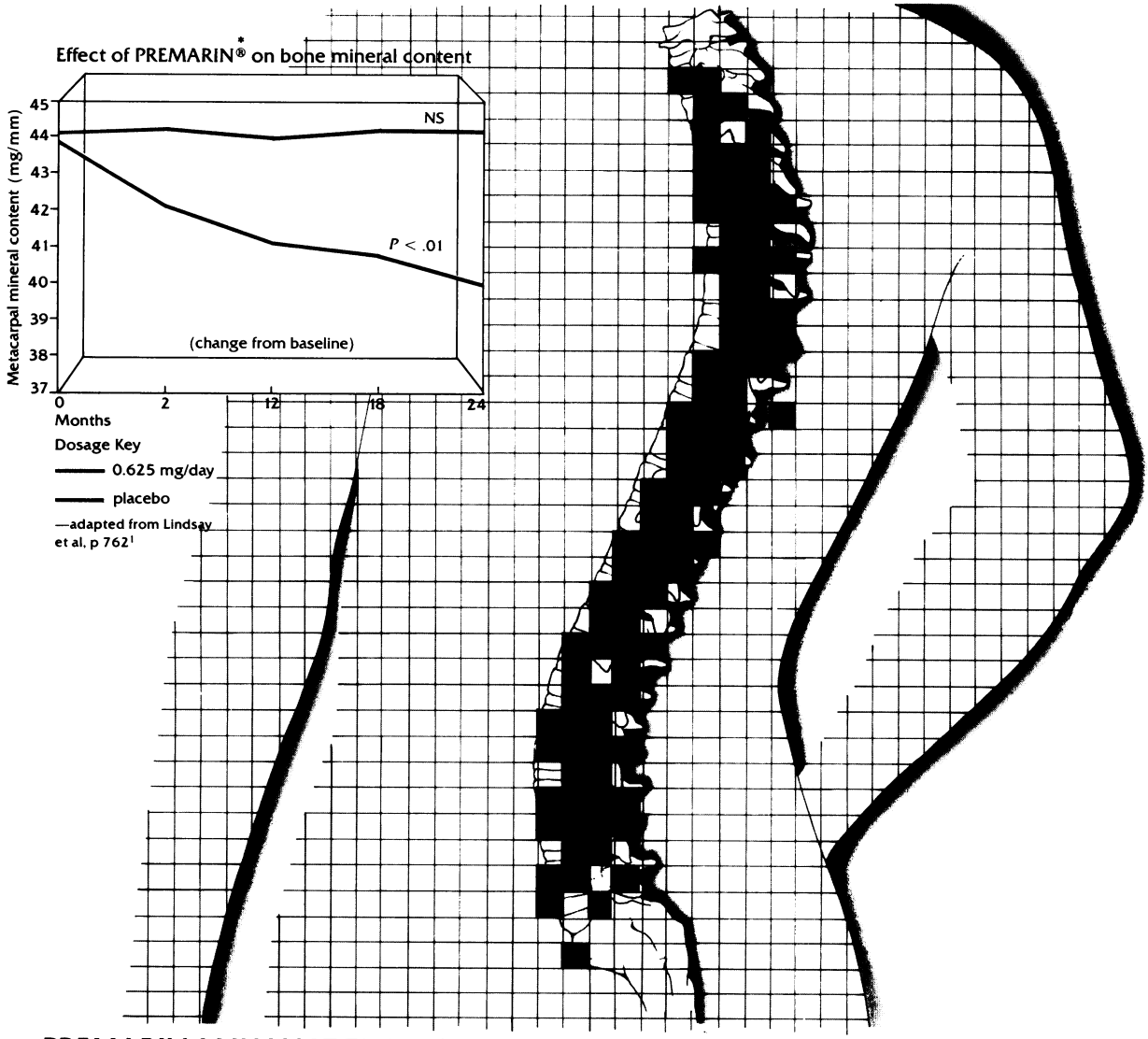
Please see last page for brief summary of full prescribing information.

POSTMENOPAUSAL BONE LOSS THAT INCAPACITATES



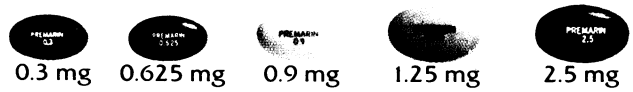
PREMARIN MAY HALT THE DISABLING COURSE OF OSTEOPOROSIS*

Osteoporosis has an enormous epidemiological impact: it affects 10 million American women, and 26% of all women over age 60.[2] The disease begins silently and progresses inexorably for 15 to 20 years, until disabling complications occur.[3]

To minimize osteoporotic damage, the condition must be detected early and treated promptly. For many patients, PREMARIN is optimal therapy for osteoporosis, as part of a comprehensive program that includes exercise, good nutrition, and calcium supplements. In a controlled study of postmenopausal and oophorectomized women, PREMARIN (Conjugated Estrogens Tablets, U.S.P.) doses of 0.625 mg/day prevented loss of metacarpal mineral content (see graph above).

PREMARIN®

(CONJUGATED ESTROGENS TABLETS, U.S.P.)



0.3 mg 0.625 mg 0.9 mg 1.25 mg 2.5 mg

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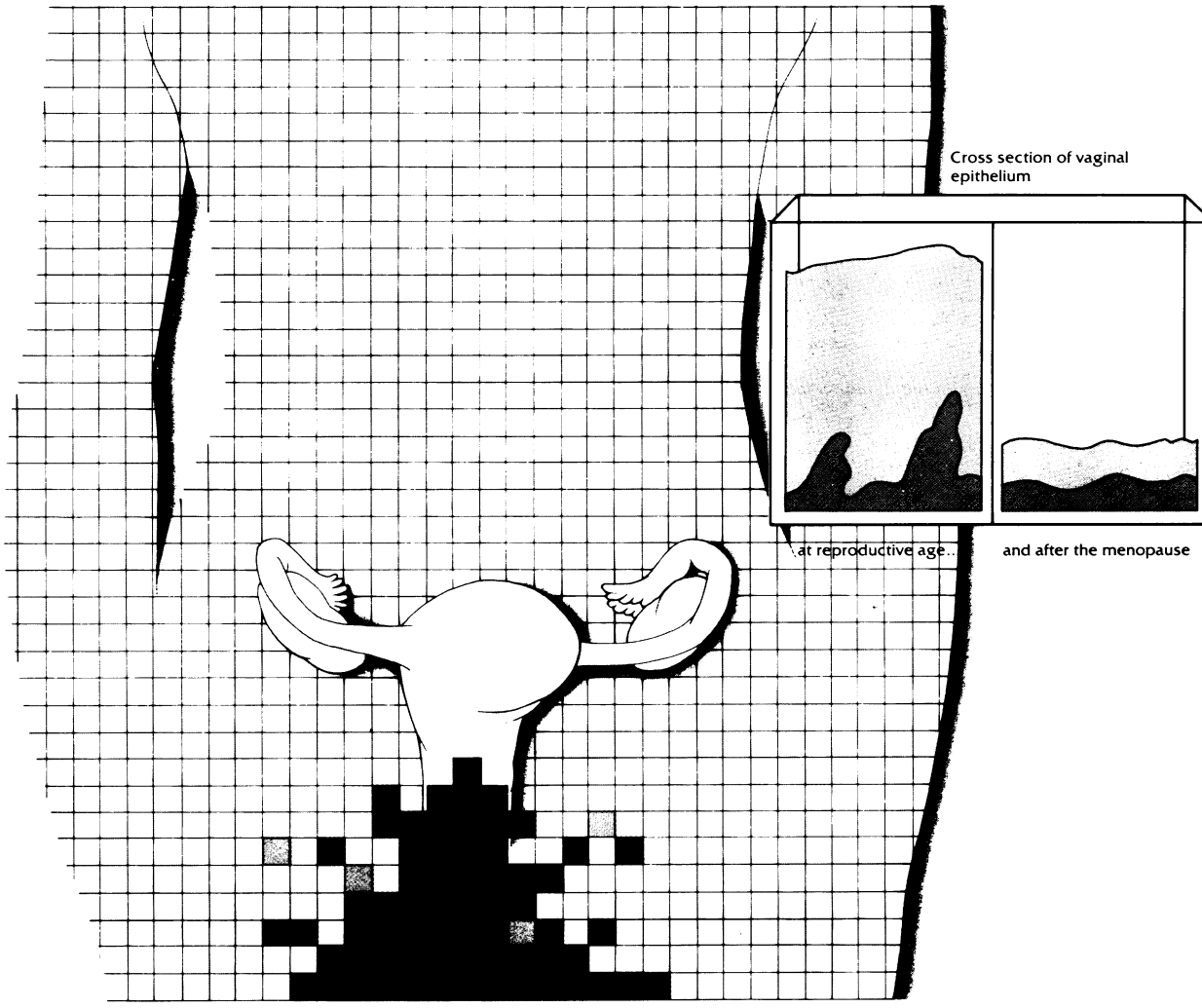
*Conjugated Estrogens Tablets have been evaluated as probably effective for estrogen-deficiency-induced osteoporosis.

Please see last page for brief summary of full prescribing information.

VAGINAL ATROPHY THAT INTERFERES WITH SEXUALITY



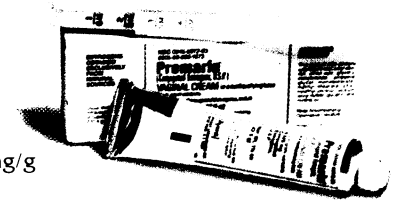
PREMARIN RESTORES THE VAGINAL ENVIRONMENT

In the postmenopausal woman, decreasing levels of estrogen can have devastating effects on a woman's sexual functioning. The pH of vaginal secretions rises, promoting the growth of contaminating organisms. The vaginal epithelium dries and thins, becoming susceptible to irritation, injury, and infection. Sexual relations may be difficult or impossible.

PREMARIN (Conjugated Estrogens, U.S.P.) Vaginal Cream focuses therapy at the site of the problem. Vaginal dryness is relieved, pH reverts to its normal acidity, and the epithelium thickens and becomes more resistant to injury and infection. With the vaginal environment returned to its premenopausal state, sexual function may improve.

PREMARIN®

(CONJUGATED ESTROGENS, U.S.P.) Vaginal Cream



0.625 mg/g

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Please see last page for brief summary of full prescribing information.

BRIEF SUMMARY *(FOR FULL PRESCRIBING INFORMATION AND PATIENT INFORMATION, SEE PACKAGE CIRCULAR)*

PREMARIN® Brand of Conjugated Estrogens Tablets, U.S.P.

PREMARIN® Brand of Conjugated Estrogens, U.S.P. Vaginal Cream in a nonliquefying base

1. ESTROGENS HAVE BEEN REPORTED TO INCREASE THE RISK OF ENDOMETRIAL CARCINOMA.

Three independent case control studies have reported an increased risk of endometrial cancer in postmenopausal women exposed to exogenous estrogens for more than one year. This risk was independent of the other known risk factors for endometrial cancer. These studies are further supported by the finding that incidence rates of endometrial cancer have increased sharply since 1969 in eight different areas of the United States with population-based cancer reporting systems, an increase which may be related to the rapidly expanding use of estrogens during the last decade. The three case control studies reported that the risk of endometrial cancer in estrogen users was about 4.5 to 13.9 times greater than in nonusers. The risk appears to depend on both duration of treatment and on estrogen dose. In view of these findings, when estrogens are used for the treatment of menopausal symptoms, the lowest dose that will control symptoms should be utilized and medication should be discontinued as soon as possible. When prolonged treatment is medically indicated, the patient should be reassessed on at least a semiannual basis to determine the need for continued therapy. Although the evidence must be considered preliminary, one study suggests that cyclic administration of low doses of estrogen may carry less risk than continuous administration; it therefore appears prudent to utilize such a regimen. Close clinical surveillance of all women taking estrogens is important. In all cases of undiagnosed persistent or recurring abnormal vaginal bleeding, adequate diagnostic measures should be undertaken to rule out malignancy. There is no evidence at present that "natural" estrogens are more or less hazardous than "synthetic" estrogens at equiestrogenic doses.

2. ESTROGENS SHOULD NOT BE USED DURING PREGNANCY.

The use of female sex hormones, both estrogens and progestogens, during early pregnancy may seriously damage the offspring. It has been shown that females exposed in utero to diethylstilbestrol, a non-steroidal estrogen, have an increased risk of developing in later life a form of vaginal or cervical cancer that is ordinarily extremely rare. This risk has been estimated as not greater than 4 per 1000 exposures. Furthermore, a high percentage of such exposed women (from 30 to 90 percent) have been found to have vaginal adenosis, epithelial changes of the vagina and cervix. Although these changes are histologically benign, it is not known whether they are precursors of malignancy. Although similar data are not available with the use of other estrogens, it cannot be presumed they would not induce similar changes. Several reports suggest an association between intrauterine exposure to female sex hormones and congenital anomalies, including congenital heart defects and limb reduction defects. One case control study estimated a 4.7-fold increased risk of limb reduction defects in infants exposed in utero to sex hormones (oral contraceptives, hormone withdrawal tests for pregnancy, or attempted treatment for threatened abortion). Some of these exposures were very short and involved only a few days of treatment. The data suggest that the risk of limb reduction defects in exposed fetuses is somewhat less than 1 per 1000. In the past, female sex hormones have been used during pregnancy in an attempt to treat threatened or habitual abortion. There is considerable evidence that estrogens are ineffective for these indications, and there is no evidence from well controlled studies that progestogens are effective for these uses. If PREMARIN is used during pregnancy, or if the patient becomes pregnant while taking this drug, she should be apprised of the potential risks to the fetus, and the advisability of pregnancy continuation.

DESCRIPTION: PREMARIN (Conjugated Estrogens, U.S.P.) contains a mixture of estrogens, obtained exclusively from natural sources, blended to represent the average composition of material derived from pregnant mares' urine. It contains estrone, equilin, and 17α-dihydroequilin, together with smaller amounts of 17α-estradiol, equilenin, and 17α-dihydroequilenin as salts of their sulfate esters.

INDICATIONS: Based on a review of PREMARIN Tablets by the National Academy of Sciences – National Research Council and/or other information, FDA has classified the indications for use as follows:

Effective: 1. Moderate to severe vasomotor symptoms associated with the menopause. (There is no evidence that estrogens are effective for nervous symptoms or depression without associated vasomotor symptoms, and they should not be used to treat such conditions.)

2. Atrophic vaginitis
3. Kraurosis vulvae
4. Female hypogonadism
5. Female castration
6. Primary ovarian failure
7. Breast cancer (for palliation only) in appropriately selected women and men with metastatic disease.
8. Prostatic carcinoma – palliative therapy of advanced disease.
9. Postpartum breast engorgement – Although estrogens have been widely used for the prevention of postpartum breast engorgement, controlled studies have demonstrated that the incidence of significant painful engorgement in patients not receiving such hormonal therapy is low and usually responsive to appropriate analgesic or other supportive therapy. Consequently, the benefit to be derived from estrogen therapy for this indication must be carefully weighed against the potential increased risk of puerperal thromboembolism associated with the use of large doses of estrogens.

PREMARIN HAS NOT BEEN SHOWN TO BE EFFECTIVE FOR ANY PURPOSE DURING PREGNANCY AND ITS USE MAY CAUSE SEVERE HARM TO THE FETUS (SEE BOXED WARNING).

"Probably" effective: For estrogen deficiency-induced osteoporosis, and only when used in conjunction with other important therapeutic measures such as diet, calcium, physiotherapy, and good general health-promoting measures. Final classification of this indication requires further investigation.

INDICATIONS: PREMARIN (Conjugated Estrogens, U.S.P.) Vaginal Cream is indicated in the treatment of atrophic vaginitis and kraurosis vulvae. PREMARIN Vaginal Cream HAS NOT BEEN SHOWN TO BE EFFECTIVE FOR ANY PURPOSE DURING PREGNANCY AND ITS USE MAY CAUSE SEVERE HARM TO THE FETUS (SEE BOXED WARNING).

CONTRAINDICATIONS: Estrogens should not be used in women (or men) with any of the following conditions: 1. Known or suspected cancer of the breast except in appropriately selected patients being treated for metastatic disease. 2. Known or suspected estrogen-dependent neoplasia. 3. Known or suspected pregnancy (See Boxed Warning). 4. Undiagnosed abnormal genital bleeding. 5. Active thrombophlebitis or thromboembolic disorders. 6. A past history of thrombophlebitis, thrombosis, or thromboembolic disorders associated with previous estrogen use (except when used in treatment of breast or prostatic malignancy).

WARNINGS: Long term continuous administration of natural and synthetic estrogens in certain animal species increases the frequency of carcinomas of the breast, cervix, vagina, and liver. There are now reports that estrogens increase the risk of carcinoma of the endometrium in humans. (See Boxed Warning.) At the present time there is no satisfactory evidence that estrogens given to postmenopausal women increase the risk of cancer of the breast, although a recent study has raised this possibility. There is a need for caution in prescribing estrogens for women with a strong family history of breast cancer or who have breast nodules, fibrocystic disease, or abnormal mammograms. A recent study has reported a 2- to 3-fold increase in the risk of surgically confirmed gallbladder disease in women receiving postmenopausal estrogens.

Adverse effects of oral contraceptives may be expected at the larger doses of estrogen used to treat prostatic or breast cancer or postpartum breast engorgement; it has been shown that there is an increased risk of thrombosis in men receiving estrogens for prostatic cancer and women for postpartum breast engorgement. Users of oral contraceptives have an increased risk of diseases, such as thrombophlebitis, pulmonary embolism, stroke, and myocardial infarction. Cases of retinal thrombosis, mesenteric thrombosis, and optic neuritis have been reported in oral contraceptive users. An increased risk of postsurgery thromboembolic complications has also been reported in users of oral contraceptives. If feasible, estrogen should be discontinued at least 4 weeks before surgery of the type associated with an increased risk of thromboembolism, or during periods of prolonged immobilization. Estrogens should not be used in persons with active thrombophlebitis, thromboembolic disorders, or in persons with a history of such disorders in association with estrogen use. They should be used with caution in patients with cerebral vascular or coronary artery disease. Large doses (5 mg conjugated estrogens per day), comparable to those used to treat cancer of the prostate and breast have been shown to increase the risk of nonfatal myocardial infarction, pulmonary embolism and thrombophlebitis. When doses of this size are used, any of the thromboembolic and thrombotic adverse effects should be considered a clear risk.

Benign hepatic adenomas should be conisidered in estrogen users having abdominal pain and tenderness, abdominal mass, or hypovolemic shock. Hepatocellular carcinoma has been reported in women taking estrogen-containing oral contraceptives. Increased blood pressure may occur with use of estrogens in the menopause and blood pressure should be monitored with estrogen use. A worsening of glucose tolerance has been observed in patients on estrogen-containing oral contraceptives. For this reason, diabetic patients should be carefully observed. Estrogens may lead to severe hypercalcemia in patients with breast cancer and bone metastases.

PRECAUTIONS: Physical examination and a complete medical and family history should be taken prior to the initiation of any estrogen therapy with special reference to blood pressure, breasts, abdomen, and pelvic organs, and should include a Papanicolau smear. As a general rule, estrogen should not be prescribed for longer than one year without another physical examination being performed. Conditions influenced by fluid retention such as asthma, epilepsy, migraine, and cardiac or renal dysfunction, require careful observation. Certain patients may develop manifestations of excessive estrogenic stimulation, such as abnormal or excessive uterine bleeding, mastodynia, etc. Prolonged administration of unopposed estrogen therapy has been reported to increase the risk of endometrial hyperplasia in some patients. Oral contraceptives appear to be associated with an increased incidence of mental depression. Patients with a history of depression should be carefully observed. Preexisting uterine leiomyomata may increase in size during estrogen use. The pathologist should be advised of estrogen therapy when relevant specimens are submitted. If jaundice develops in any patient receiving estrogen, the medication should be discontinued while the cause is investigated. Estrogens should be used with care in patients with impaired liver function, renal insufficiency, metabolic bone diseases associated with hypercalcemia, or in young patients in whom bone growth is not complete.

The following changes may be expected with larger doses of estrogen:

a. Increased sulfobromophthalein retention.

b. Increased prothrombin and factors VII, VIII, IX, and X; decreased antithrombin 3; increased norepinephrine-induced platelet aggregability.

c. Increased thyroid binding globulin (TBG) leading to increased circulating total thyroid hormone, as measured by PBI, T4 by column, or T4 by radioimmunoassay. Free T3 resin uptake is decreased, reflecting the elevated TBG; free T4 concentration is unaltered.

d. Impaired glucose tolerance.

e. Decreased pregnanediol excretion.

f. Reduced response to metyrapone test.

g. Reduced serum folate concentration.

h. Increased serum triglyceride and phospholipid concentration.

As a general principle, the administration of any drug to nursing mothers should be done only when clearly necessary since many drugs are excreted in human milk.

ADVERSE REACTIONS: The following have been reported with estrogenic therapy, including oral contraceptives: breakthrough bleeding, spotting, change in menstrual flow; dysmenorrhea; premenstrual-like syndrome; amenorrhea during and after treatment; increase in size of uterine fibromyomata; vaginal candidiasis, change in cervical erosion and in degree of cervical secretion; cystitis-like syndrome; tenderness, enlargement, secretion (of breasts); nausea, vomiting, abdominal cramps, bloating; cholestatic jaundice; chloasma or melasma which may persist when drug is discontinued; erythema multiforme; erythema nodosum; hemorrhagic eruption; loss of scalp hair; hirsutism; steepening of corneal curvature; intolerance to contact lenses; headache, migraine, dizziness, mental depression, chorea; increase or decrease in weight; reduced carbohydrate tolerance; aggravation of porphyria; edema; changes in libido.

ACUTE OVERDOSAGE: May cause nausea, and withdrawal bleeding may occur in females.

DOSAGE AND ADMINISTRATION:

PREMARIN® Brand of Conjugated Estrogens Tablets, U.S.P.

1. *Given cyclically for short-term use only.* For treatment of moderate to severe *vasomotor* symptoms, atrophic vaginitis, or kraurosis vulvae associated with the menopause (0.3 to 1.25 mg or more daily).

The lowest dose that will control symptoms should be chosen and medication should be discontinued as promptly as possible.

Administration should be cyclic (*e.g.*, three weeks on and one week off).

Attempts to discontinue or taper medication should be made at three to six month intervals.

2. *Given cyclically:* Female hypogonadism. Female castration. Primary ovarian failure. Osteoporosis.

Female hypogonadism – 2.5 to 7.5 mg daily, in divided doses for 20 days, followed by a rest period of 10 days' duration. If bleeding does not occur by the end of this period, the same dosage schedule is repeated. The number of courses of estrogen therapy necessary to produce bleeding may vary depending on the responsiveness of the endometrium.

If bleeding occurs before the end of the 10 day period, begin a 20 day estrogen-progestin cyclic regimen with PREMARIN (Conjugated Estrogens Tablets, U.S.P.), 2.5 to 7.5 mg daily in divided doses, for 20 days. During the last five days of estrogen therapy, give an oral progestin. If bleeding occurs before this regimen is concluded, therapy is discontinued and may be resumed on the fifth day of bleeding.

Female castration and primary ovarian failure – 1.25 mg daily, cyclically. Adjust upward or downward according to response of the patient. For maintenance, adjust dosage to lowest level that will provide effective control.

Osteoporosis (to retard progression) – 1.25 mg daily, cyclically.

3. *Given for a few days:* Prevention of postpartum breast engorgement – 3.75 mg every four hours for five doses, or 1.25 mg every four hours for five days.

4. *Given chronically:* Inoperable progressing prostatic cancer – 1.25 to 2.5 mg three times daily.

Inoperable progressing breast cancer in appropriately selected men and postmenopausal women – 10 mg three times daily for a period of at least three months.

Patients with an intact uterus should be monitored for signs of endometrial cancer and appropriate measures taken to rule out malignancy in the event of persistent or recurring abnormal vaginal bleeding.

PREMARIN® Brand of Conjugated Estrogens, U.S.P. Vaginal Cream

Given cyclically for short-term use only. For treatment of atrophic vaginitis or kraurosis vulvae.

The lowest dose that will control symptoms should be chosen and medication should be discontinued as promptly as possible.

Administration should be cyclic (*e.g.*, three weeks on and one week off).

Attempts to discontinue or taper medication should be made at three to six month intervals.

Usual dosage range: 2 to 4 g daily, intravaginally or topically, depending on the severity of the condition.

Treated patients with an intact uterus should be monitored closely for signs of endometrial cancer and appropriate diagnostic measures should be taken to rule out malignancy in the event of persistent or recurring abnormal vaginal bleeding.

HOW SUPPLIED: PREMARIN (Conjugated Estrogens Tablets, U.S.P.). No. 865 Each *purple* tablet contains 2.5 mg in bottles of 100 and 1,000. No. 866 Each *yellow* tablet contains 1.25 mg in bottles of 100 and 1,000. Also in Cycle Pack of 21 and in unit dose package of 100. No. 864 Each *white* tablet contains 0.9 mg in bottles of 100. Also in Cycle Pack of 21. No. 867 Each *maroon* tablet contains 0.625 mg in bottles of 100 and 1,000. Also in Cycle Pack of 21 and unit dose package of 100. No. 868 Each *green* tablet contains 0.3 mg in bottles of 100 and 1,000. The appearance of these tablets is a trademark of Ayerst Laboratories.

PREMARIN (Conjugated Estrogens, U.S.P.) Vaginal Cream No. 872 Each gram contains 0.625 mg Conjugated Estrogens, U.S.P. (Also contains cetyl esters wax, cetyl alcohol, white wax, glyceryl monostearate, propylene glycol monostearate, methyl stearate, phenylethyl alcohol, sodium lauryl sulfate, glycerin, and mineral oil.)

Combination package: Each contains Net Wt. 1½ oz. (42.5 g) tube with one calibrated plastic applicator.

Also Available - Refill package: Each contains Net Wt. 1½ oz. (42.5 g) tube. **4340R1/285**

References: 1. Lindsay R, Hart DM, Clark DM: The minimum effective dose of estrogen for prevention of postmenopausal bone loss. *Obstet Gynecol* 1984;63:759-763. **2.** Katz WA: *Rheumatic Diseases: Diagnosis and Management*. Philadelphia, JB Lippincott Co, 1977, p 672. **3.** Reese WD: A better way to screen for osteoporosis. *Contemp Ob/Gyn* 1983;22(November):116-131. **4.** Judd HL: After the menopause. *Transition* 1983;1:19-30. **5.** Erlik Y, Tataryn IV, Meldrum DR, et al: Association of waking episodes with menopausal hot flushes. *JAMA* 1981;245:1741-1744. **6.** Meldrum DR: The pathophysiology of postmenopausal symptoms. *Sem Reprod Endocrinol* 1983;1(February):11-17.

Ayerst® AYERST LABORATORIES
New York, N.Y. 10017

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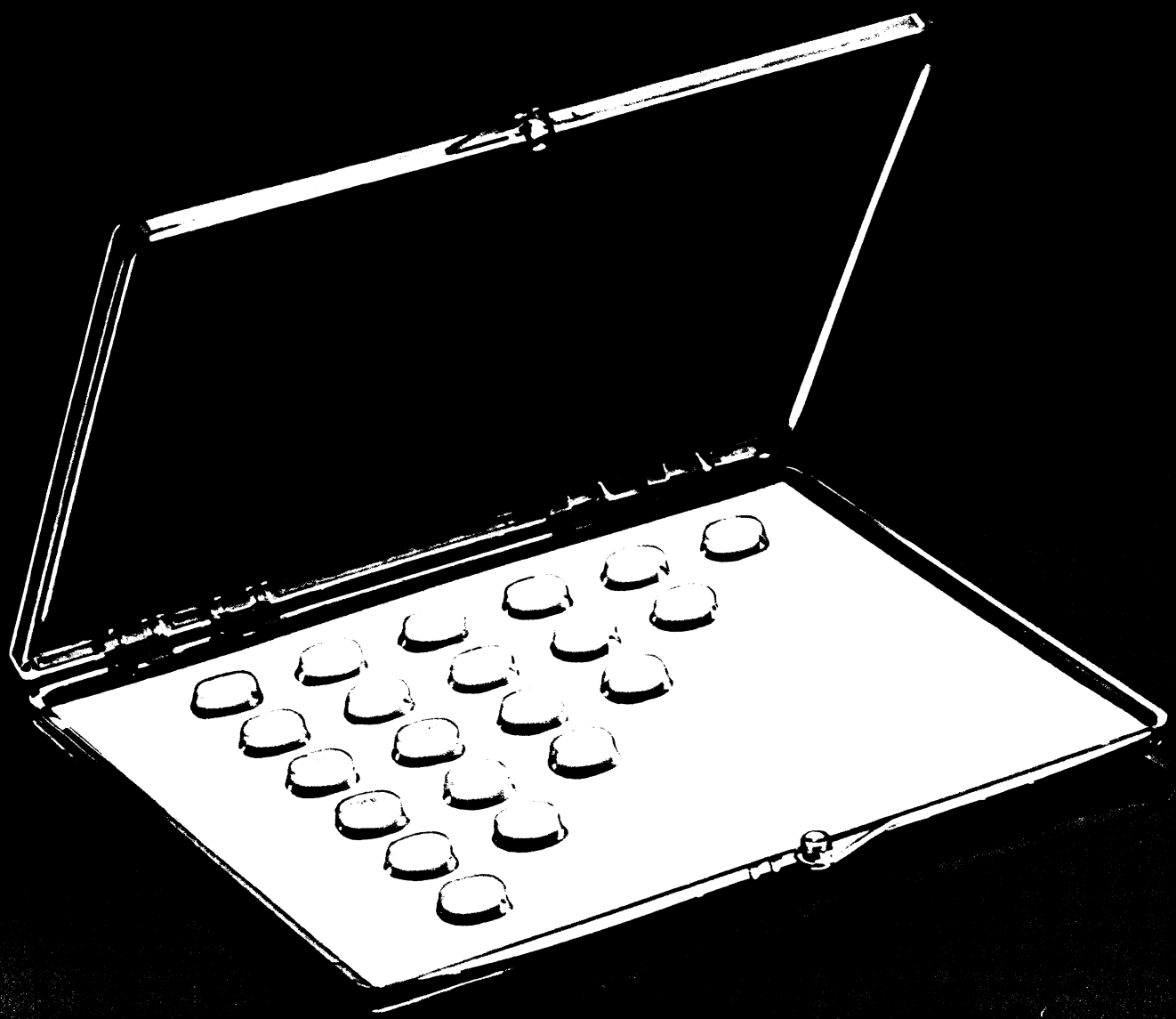
Medrol Dosepak Unit-of-Use

4 mg methylprednisolone tablets, USP

The explicit printed dosage instructions that accompany each *Dosepak* make it easy for the patient to understand and follow the dosage regimen.



"When it comes to cardiovascular medicine, I like to know exactly what my patients are swallowing."

There are doctors who say that generic drugs have a place in their practice—but not necessarily in the treatment of serious or potentially life-threatening disease. And when they consider that the average patient pays only about 45¢ a day for INDERAL (propranolol HCl) Tablets, there's not much left to discuss.

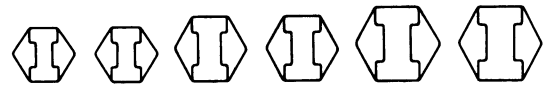
When it's INDERAL Tablets you want for the treatment of hypertension, angina, arrhythmias, or post-MI patients, make sure you specify "Dispense As Written" (DAW), "Do Not Substitute," or whatever is required in your State. That way, you'll know exactly what your patients will get.

Please see next page for brief summary of prescribing information.

"When it comes to cardiovascular medicine, I like to know exactly what my patients are swallowing."

INDERAL® *Tablets*

BRAND OF PROPRANOLOL HCl



10 mg 20 mg 40 mg 60 mg 80 mg 90 mg*

BRIEF SUMMARY (FOR FULL PRESCRIBING INFORMATION, SEE PACKAGE CIRCULAR.)

INDERAL® (propranolol hydrochloride) Tablets

CONTRAINDICATIONS

INDERAL is contraindicated in 1) cardiogenic shock, 2) sinus bradycardia and greater than first degree block, 3) bronchial asthma, 4) congestive heart failure (see WARNINGS) unless the failure is secondary to a tachyarrhythmia treatable with INDERAL.

WARNINGS

CARDIAC FAILURE: Sympathetic stimulation may be a vital component supporting circulatory function in patients with congestive heart failure, and its inhibition by beta blockade may precipitate more severe failure. Although beta blockers should be avoided in overt congestive heart failure, if necessary they can be used with close follow-up in patients with a history of failure who are well compensated and are receiving digitalis and diuretics. Beta-adrenergic blocking agents do not abolish the inotropic action of digitalis on heart muscle.

IN PATIENTS WITHOUT A HISTORY OF HEART FAILURE, continued use of beta blockers can, in some cases, lead to cardiac failure. Therefore, at the first sign or symptom of heart failure, the patient should be digitalized and/or treated with diuretics, and the response observed closely, or INDERAL should be discontinued (gradually, if possible).

IN PATIENTS WITH ANGINA PECTORIS, there have been reports of exacerbation of angina and, in some cases, myocardial infarction, following abrupt discontinuance of INDERAL therapy. Therefore, when discontinuance of INDERAL is planned the dosage should be gradually reduced over at least a few weeks and the patient should be cautioned against interruption or cessation of therapy without the physician's advice. If INDERAL therapy is interrupted and exacerbation of angina occurs, it usually is advisable to reinstitute INDERAL therapy and take other measures appropriate for the management of unstable angina pectoris. Since coronary artery disease may be unrecognized, it may be prudent to follow the above advice in patients considered at risk of having occult atherosclerotic heart disease who are given propranolol for other indications.

Nonallergic Bronchospasm (e.g., chronic bronchitis, emphysema)— PATIENTS WITH BRONCHOSPASTIC DISEASES SHOULD IN GENERAL NOT RECEIVE BETA BLOCKERS. INDERAL should be administered with caution since it may block bronchodilation produced by endogenous and exogenous catecholamine stimulation of beta receptors.

MAJOR SURGERY: The necessity or desirability of withdrawal of beta-blocking therapy prior to major surgery is controversial. It should be noted, however, that the impaired ability of the heart to respond to reflex adrenergic stimuli may augment the risks of general anesthesia and surgical procedures.

INDERAL, like other beta blockers, is a competitive inhibitor of beta-receptor agonists and its effects can be reversed by administration of such agents, e.g., dobutamine or isoproterenol. However, such patients may be subject to protracted severe hypotension. Difficulty in starting and maintaining the heartbeat has also been reported with beta blockers.

DIABETES AND HYPOGLYCEMIA: Beta-adrenergic blockade may prevent the appearance of certain premonitory signs and symptoms (pulse rate and pressure changes) of acute hypoglycemia in labile insulin-dependent diabetes. In these patients, it may be more difficult to adjust the dosage of insulin.

THYROTOXICOSIS: Beta blockade may mask certain clinical signs of hyperthyroidism. Therefore, abrupt withdrawal of propranolol may be followed by an exacerbation of symptoms of hyperthyroidism, including thyroid storm. Propranolol does not distort thyroid function tests.

IN PATIENTS WITH WOLFF-PARKINSON-WHITE SYNDROME, several cases have been reported in which, after propranolol, the tachycardia was replaced by a severe bradycardia requiring a demand pacemaker. In one case this resulted after an initial dose of 5 mg propranolol.

PRECAUTIONS

General: Propranolol should be used with caution in patients with impaired hepatic or renal function. INDERAL is not indicated for the treatment of hypertensive emergencies.

Beta-adrenoreceptor blockade can cause reduction of intraocular pressure. Patients should be told that INDERAL (propranolol hydrochloride) may interfere with the glaucoma screening test. Withdrawal may lead to a return of increased intraocular pressure.

Clinical Laboratory Tests: Elevated blood urea levels in patients with severe heart disease, elevated serum transaminase, alkaline phosphatase, lactate dehydrogenase.

DRUG INTERACTIONS: Patients receiving catecholamine-depleting drugs such as reserpine should be closely observed if INDERAL is administered. The added catecholamine-blocking action may produce an excessive reduction of resting sympathetic nervous activity which may result in hypotension, marked bradycardia, vertigo, syncopal attacks, or orthostatic hypotension.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term studies in animals have been conducted to evaluate toxic effects and carcinogenic potential. In 18-month studies in both rats and mice, employing doses up to 150 mg/kg/day, there was no evidence of significant drug-induced toxicity. There were no drug-related tumorigenic effects at any of the dosage levels. Reproductive studies in animals did not show any impairment of fertility that was attributable to the drug.

Pregnancy: Pregnancy Category C. INDERAL has been shown to be embryotoxic in animal studies at doses about 10 times greater than the maximum recommended human dose.

There are no adequate and well-controlled studies in pregnant women. INDERAL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: INDERAL is excreted in human milk. Caution should be exercised when INDERAL is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Most adverse effects have been mild and transient and have rarely required the withdrawal of therapy.

Cardiovascular: bradycardia; congestive heart failure; intensification of AV block; hypotension; paresthesia of hands; thrombocytopenic purpura; arterial insufficiency, usually of the Raynaud type.

Central Nervous System: Lightheadedness; mental depression manifested by insomnia, lassitude, weakness, fatigue; reversible mental depression progressing to catatonia; visual disturbances; hallucinations; an acute reversible syndrome characterized by disorientation for time and place, short-term memory loss, emotional lability, slightly clouded sensorium, and decreased performance on neuropsychometrics.

Gastrointestinal: nausea, vomiting, epigastric distress, abdominal cramping, diarrhea, constipation, mesenteric arterial thrombosis, ischemic colitis.

Allergic: pharyngitis and agranulocytosis, erythematous rash, fever combined with aching and sore throat, laryngospasm and respiratory distress.

Respiratory: bronchospasm.

Hematologic: agranulocytosis, nonthrombocytopenic purpura, thrombocytopenic purpura.

Auto-Immune: In extremely rare instances, systemic lupus erythematosus has been reported.

Miscellaneous: alopecia, LE-like reactions, psoriasiform rashes, dry eyes, male impotence, and Peyronie's disease have been reported rarely. Oculomucocutaneous reactions involving the skin, serous membranes and conjunctivae reported for a beta blocker (practolol) have not been associated with propranolol.

*The appearance of INDERAL tablets is a registered trademark of Ayerst Laboratories.

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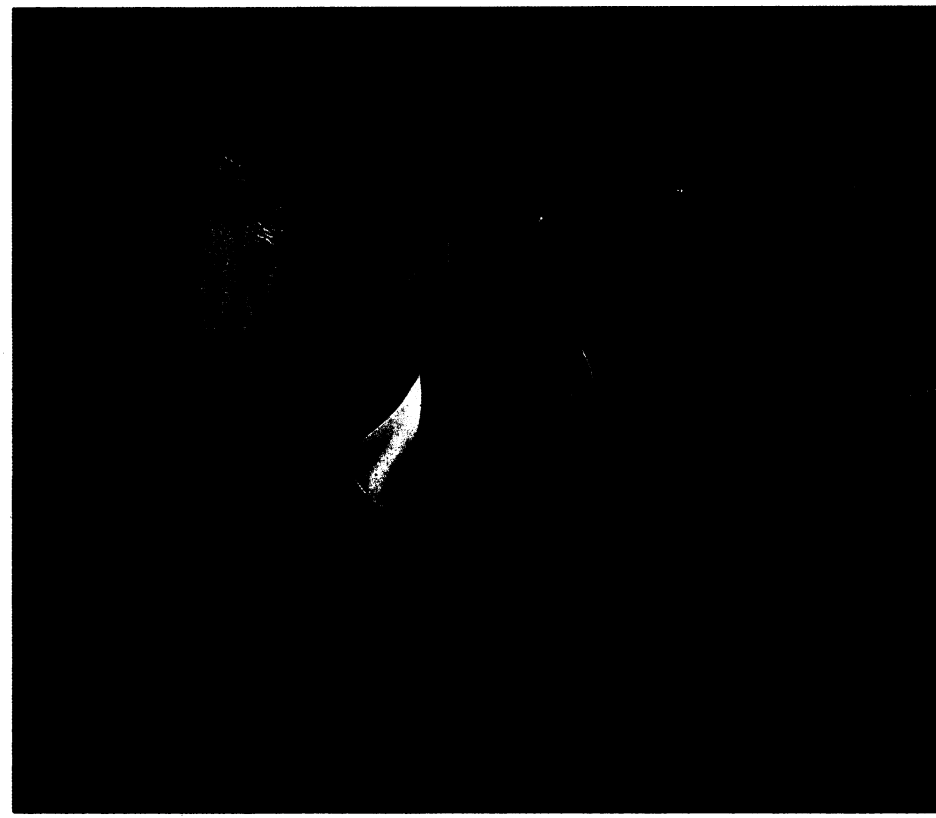
New York, N.Y. 10017

Beta Blockers Aren't for Everyone



In Hypertension*... When you need to conserve K^+

P R E S C R I B E

DYAZIDE®

25 mg Hydrochlorothiazide/**50 mg** Triamterene/SKF

For the Majority of Patient Types Over 50 ▪ Black ▪ Physically Active ▪ Asthmatic

*Not for initial therapy. See brief summary.

Serum K^+ and BUN should be checked periodically (see Warnings and Precautions).

Before prescribing, see complete prescribing information in SK&F CO. literature or *PDR*. The following is a brief summary.

* **WARNING**

This drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual. If this combination represents the dosage so determined, its use may be more convenient in patient management. Treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

Contraindications: Concomitant use with other potassium-sparing agents such as spironolactone or amiloride. Further use in anuria, progressive renal or hepatic dysfunction, hyperkalemia. Pre-existing elevated serum potassium. Hypersensitivity to either component or other sulfonamide-derived drugs.

Warnings: Do not use potassium supplements, dietary or otherwise, unless hypokalemia develops or dietary intake of potassium is markedly impaired. If supplementary potassium is needed, potassium tablets should not be used. Hyperkalemia can occur, and has been associated with cardiac irregularities. It is more likely in the severely ill, with urine volume less than one liter/day, the elderly and diabetics with suspected or confirmed renal insufficiency. Periodically, serum K^+ levels should be determined. If hyperkalemia develops, substitute a thiazide alone, restrict K^+ intake. **Associated widened QRS complex or arrhythmia requires prompt additional therapy.** Thiazides cross the placental barrier and appear in cord blood. Use in pregnancy requires weighing anticipated benefits against possible hazards, including fetal or neonatal jaundice, thrombocytopenia, other adverse reactions seen in adults. Thiazides appear and triamterene may appear in breast milk. If their use is essential, the patient should stop nursing. Adequate information on use in children is not available. Sensitivity reactions may occur in patients with or without a history of allergy or bronchial asthma. Possible exacerbation or activation of systemic lupus erythematosus has been reported with thiazide diuretics.

Precautions: The bioavailability of the hydrochlorothiazide component of 'Dyazide' is about 50% of the bioavailability of the single entity. Theoretically, a patient transferred from the single entities of Dyrenium (triamterene, SK&F CO.) and hydrochlorothiazide may show an increase in blood pressure or fluid retention. Similarly, it is also possible that the lesser hydrochlorothiazide bioavailability could lead to increased serum potassium levels. However, extensive clinical experience with 'Dyazide' suggests that these conditions have not been commonly observed in clinical practice. Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids, and during concurrent use with amphotericin B or corticosteroids or corticotropin [ACTH]). Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics or those with suspected or confirmed renal insufficiency. Cumulative effects of the drug may develop in patients with impaired renal function. Thiazides should be used with caution in patients with impaired hepatic function. They can precipitate coma in patients with severe liver disease. Observe regularly for possible blood dyscrasias, liver damage, other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving triamterene, and leukopenia, thrombocytopenia, agranulocytosis, and aplastic and hemolytic anemia have been reported with thiazides. Thiazides may cause manifestation of latent diabetes mellitus. The effects of oral anticoagulants may be decreased when used concurrently with hydrochlorothiazide; dosage adjustments may be necessary. Clinically insignificant reductions in arterial responsiveness to norepinephrine have been reported. Thiazides have also been shown to increase the paralyzing effect of nondepolarizing muscle relaxants such as tubocurarine. Triamterene is a weak folic acid antagonist. Do periodic blood studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in post-sympathectomy patients. Use cautiously in surgical patients. Triamterene has been found in renal stones in association with the other usual calculus components. Therefore, 'Dyazide' should be used with caution in patients with histories of stone formation. A few occurrences of acute renal failure have been reported in patients on 'Dyazide' when treated with indomethacin. Therefore, caution is advised in administering nonsteroidal anti-inflammatory agents with 'Dyazide'. The following may occur: transient elevated BUN or creatinine or both, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), hyperuricemia and gout, digitalis intoxication (in hypokalemia), decreasing alkali reserve with possible metabolic acidosis. 'Dyazide' interferes with fluorescent measurement of quinidine. Hypokalemia is uncommon with 'Dyazide', but should it develop, corrective measures should be taken such as potassium supplementation or increased dietary intake of potassium-rich foods. Corrective measures should be instituted cautiously and serum potassium levels determined. Discontinue corrective measures and 'Dyazide' should laboratory values reveal elevated serum potassium. Chloride deficit may occur as well as dilutional hyponatremia. Concurrent use with chlorpropamide may increase the risk of severe hyponatremia. Serum PBI levels may decrease without signs of thyroid disturbance. Calcium excretion is decreased by thiazides. 'Dyazide' should be withdrawn before conducting tests for parathyroid function.

Thiazides may add to or potentiate the action of other antihypertensive drugs.

Diuretics reduce renal clearance of lithium and increase the risk of lithium toxicity.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis, rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting, diarrhea, constipation, other gastrointestinal disturbances; postural hypotension (may be aggravated by alcohol, barbiturates, or narcotics). Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and respiratory distress including pneumonitis and pulmonary edema, transient blurred vision, sialadenitis, and vertigo have occurred with thiazides alone. Triamterene has been found in renal stones in association with other usual calculus components. Rare incidents of acute interstitial nephritis have been reported. Impotence has been reported in a few patients on 'Dyazide', although a causal relationship has not been established.

Supplied: 'Dyazide' is supplied as a red and white capsule, in bottles of 1000 capsules; Single Unit Packages (unit-dose) of 100 (intended for institutional use only); in Patient-Pak™ unit-of-use bottles of 100.

BRS-DZ:L39

a product of

SK&F CO.

Carolina, P.R. 00630

The unique red and white Dyazide® capsule: Your assurance of SK&F quality.

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NEVADA STATE MEDICAL ASSOCIATION
1985 ANNUAL CONVENTION & SCIENTIFIC SESSION

May 9-12, 1985 □ Hyatt Lake Tahoe □ Incline Village, NV

SCIENTIFIC SESSION

Friday, May 10

Program Chairman: John J. Stapleton, M.D.

8:00 am	**Introductions** *Anton Sohn, M.D.* President, Nevada State Medical Association
8:15 am	**"Surgical Management—Breast Carcinoma"** *James E. Goodnight, M.D., Ph.D.* U.C. Davis Medical Center
9:00 am	**"Chemotherapy—Breast Carcinoma"** *Richard J. Cohen, M.D.* U.C. San Francisco School of Medicine
9:45 am	Questions & Answers—Panel *Drs. Goodnight and Cohen*
10:00 am	Refreshment Break
10:15 am	**"Corneal Complications of Extracapsular Cataract Extractions and Intraocular Lens Implantation"** *Robert G. Webster, M.D.* Pacific Medical Center, San Francisco
11:00 am	**"Breast Reconstruction"** *Stephen J. Mathes, M.D.* U.C. San Francisco School of Medicine
11:45 am	Questions & Answers—Panel *Drs. Webster and Mathes*
12:15 pm	Luncheon and presentation with NSMA Auxiliary **"Stress and the Physician"** *G. Douglas Talbott, M.D.—* *Medical Association of Georgia*
1:30 pm	**"Overview—Breast Carcinoma"** Panel: *Drs. Cohen, Goodnight, Mathes* Moderator: *H. Treat Cafferata, M.D.*
3:00 pm	Adjournment

CONVENTION SCHEDULE

Thursday, May 9

4:00 pm	NSMA Council Meeting
6:00 pm	Reception & Dinner for Council members & wives/guests

Friday, May 10

7:30 am	Continental Breakfast
8:00 am	Scientific Session
8:00 am	Auxiliary Board Meeting
9:00 am	Auxiliary Membership Meeting & Workshops
12:15 pm	Joint Luncheon
1:30 pm	Scientific Session & Auxiliary Workshops continue
3:00 pm	Adjournment of Scientific Session
3:30 pm	House of Delegates—Opening Session
5:30 pm	Cocktail Party

Saturday, May 11

7:30 am	Continental Breakfast
8:00 am	Reference Committees Auxiliary Workshops
Noon	Lunch & Afternoon Activities—on your own
4:00 pm	Nevada Chapter of American College of Surgeons—Committee on Trauma
6:00 pm	Presidents' Inaugurations & Awards Ceremony—Wine served
7:30 pm	Bavarian Bierstube—Relax, Dine, Dance & Sing in the Atmosphere of a Bavarian Beirhall!

Sunday, May 12

7:30 am	Continental Breakfast
8:00 am	House of Delegates—Closing Session
11:00 am	Adjournment

HEADQUARTERS HOTEL

THE HYATT LAKE TAHOE—Majestic High Sierras, towering pines, crystal clear waters and spacious, elegant sleeping rooms overlooking Lake Tahoe at Incline Village, Nevada. You'll discover an indoor health spa, outdoor heated pool, and an 18-station exercourse in the pine forest adjacent to the hotel. Selection of fine restaurants including Hugo's Rotisserie.

REGISTRATION

Name _____

Address _____

City/State/Zip _____

Telephone _____

Return this form along with appropriate fees to the Nevada State Medical Association, 3660 Baker Lane, Reno, NV 89509, or register by phone, (702) 825-6788, Kathleen Boyce, Convention Manager. Housing information will be forwarded upon receipt of registration.

CHECK ONE:	Before May 1	After May 1
NSMA Members		
(General Registration)		
Regular	$150	$160
Out-of-state	100	110
Retired	75	85
Resident	75	85
Student	50	60
Nonmembers		
(Scientific Session only)		
Physicians	$150	$160
Nurses	50	60

NEW MEXICO 99TH

Scientific Program

Acquired Immune Deficiency Syndrome (AIDS)
Contemporary Issues in Medical Ethics
Nuclear Magnetic Resonance

Accreditation

As an accredited organization for continuing medical education, the New Mexico Medical Society certifies that this educational offering meets the criteria for 9 credit hours in Category I of the Physicians Recognition Award of the American Medical Association. It is acceptable for 9 prescribed hours, AAFP.

WEDNESDAY, MAY 1

8:30 AM NM Physicians Mutual Liability Company—Board of Directors Meeting
10:00 AM Registration
10:30 AM NM Physicians Mutual Liability Company—Annual Meeting
2:00 PM House of Delegates—First Meeting
Guest: Alan R. Nelson, MD, Trustee, Board of Trustees, American Medical Association
3:30 PM Reference Committee Hearings
6:30 PM President's Reception and Banquet

THURSDAY, MAY 2

ACQUIRED IMMUNE DEFICIENCY SYNDROME (AIDS)

Presiding William Boehm, MD, President-Elect, NMMS
Moderator Toby Simon, MD

8:30 AM **Virology**—Gregory Mertz,MD
9:00 AM **Pathogenesis of Immune Deficiency**—Darwin L. Palmer, MD
9:25 AM **Clinical Aspects: Diagnosis and Patient Management**—Donald Romig, MD
10:00 AM **Refreshment Break**
10:30 AM **Public Health Implications in New Mexico**—Harry Hull, MD
10:50 AM **Implications for Blood Donors and Recipients**—Toby Simon, MD
11:10 AM **AIDS and the Gay Man: Fear and Action in the '80s**—James Waltner, MD
11:35 AM **Ethical Implications of AIDS**—Ronald A. Carson, PhD

MEDICAL SOCIETY ANNUAL MEETING

MAY 1-3, 1985
ALBUQUERQUE, MARRIOTT HOTEL

THURSDAY, MAY 2, CONTINUED

CONTEMPORARY ISSUES IN MEDICAL ETHICS

Presiding Edward L. Johnson, MD, Vice-President, NMMS
Moderator Robert C. Derbyshire, MD

2:00 PM **Current Problems Related to Medical Ethics**—Ronald A. Carson, PhD
2:45 PM **Case Presentation #1**—R. C. Derbyshire, MD
3:05 PM **Refreshment Break**
3:35 PM **Case Presentation #2**—Alice M. Luna, MD
4:00 PM **Panel Discussion** (written questions from both sessions)
R. A. Carson, PhD; D. L. Palmer, MD; H. Hull, MD; D. Romig, MD; Chas. Leonard, MD; Toby Simon, MD; A. M. Luna, MD; Jas. Waltner, MD; Gregory Mertz, MD, and R. C. Derbyshire, MD, Moderator
6:30 PM Past Presidents Club Banquet
Specialty Society Meetings

FRIDAY, MAY 3

NUCLEAR MAGNETIC RESONANCE

Presiding W. Marion Jordan, MD, President, NMMS
Moderator Charles M. Thompson, MD

9:00 AM **Introduction**—Charles M. Thompson, MD
9:05 AM **The Physics of Nuclear Magnetic Resonance**—William Thompson, MD
9:35 AM **Clinical Applications of NMR**—James L. Lowry, MD
10:05 AM **Refreshment Break**
10:35 AM **Future Possibilities of NMR in Clinical Diagnosis**—William Thompson, MD
11:15 AM **Panel Discussion**
W. Marion Jordan, MD; James L. Lowry, MD; William Thompson, MD, and Charles M. Thompson, MD, Moderator
12:30 PM NEMPAC Luncheon—Classic Hotel
2:00 PM House of Delegates Second Meeting

(Continued on page 586)

(Continued from page 585)

Educational Objectives

This course is designed to provide a review of current management techniques in the diagnosis and treatment of AIDS. It focuses on the social and ethical issues in the practice of medicine today. The presentation of case histories will be followed by a panel where there will be the opportunity for discussion of problems with speakers.

The symposium on nuclear magnetic resonance is oriented to physicians as a brief course on the clinical applications, diagnostic possibilities and the physics of this new technology. A panel discussion will follow.

FACULTY

Ronald A. Carson, PhD
Professor & Director, Institute for Medical Humanities, University of Texas, Medical Branch, Galveston, Texas

R. C. Derbyshire, MD
Surgeon, Emeritus, Retired Secretary, New Mexico Board of Medical Examiners, Santa Fe, New Mexico

Harry Hull, MD
Epidemiologist, New Mexico Department of Health & Environment, Santa Fe, New Mexico

W. Marion Jordan, MD
President, New Mexico Medical Society, Private Practice-Radiology, Albuquerque

Charles Leonard, MD
Private Practice, Nephrology, Attorney at Law, Albuquerque

James L. Lowry, MD
Private Practice-Radiology, Albuquerque

Alice M. Luna, MD
Private Practice-Pediatrics, Albuquerque

Gregory Mertz, MD
Department of Medicine, Infectious Disease, University of New Mexico School of Medicine, Albuquerque

Darwin L. Palmer, MD
Chief, Division of Infectious Disease, Veterans Administration Medical Center; Chief, Division of Infectious Disease, Department of Medicine, University of New Mexico School of Medicine, Albuquerque

Donald Romig, MD
Private Practice, Internal Medicine, Infectious Disease, Santa Fe, New Mexico

Toby Simon, MD
Medical Director, United Blood Services, Albuquerque

Charles Thompson, MD
Radiologist, Emeritus, Albuquerque

William Thompson, MD
Chief, Radiology, Veterans Administration Medical Center, Chapel Hill, North Carolina

James Waltner, MD
Private Practice-Pediatrics, Espanola, New Mexico

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[illegible] of angina pectoris due to coronary artery spasm. Chronic stable angina in patients who cannot take beta blockers or who remain symptomatic on adequate doses of beta blockers and/or other antianginal agents.

[illegible] and other antianginal agents in the management of [illegible]

Reduces angina attack frequency*
42% to 46% decrease reported in multicenter study.[1]

Increases exercise tolerance*
In Bruce exercise test,[2] control patients averaged 8.0 minutes to onset of pain; Cardizem patients averaged 9.8 minutes ($P<.005$).

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[illegible] prescribing information on following page.

2/84

PROFESSIONAL USE INFORMATION

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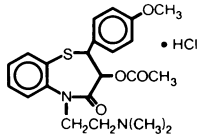
(diltiazem HCl)
30 mg and 60 mg tablets

DESCRIPTION

CARDIZEM® (diltiazem hydrochloride) is a calcium ion influx inhibitor (slow channel blocker or calcium antagonist). Chemically, diltiazem hydrochloride is 1,5-Benzothiazepin-4(5H)one,3-(acetyloxy) -5-[2-(dimethylamino)ethyl]-2,3-dihydro-2-(4-methoxyphenyl)-, monohydrochloride,(+) -cis-. The chemical structure is:



Diltiazem hydrochloride is a white to off-white crystalline powder with a bitter taste. It is soluble in water, methanol, and chloroform. It has a molecular weight of 450.98. Each tablet of CARDIZEM contains either 30 mg or 60 mg diltiazem hydrochloride for oral administration.

CLINICAL PHARMACOLOGY

The therapeutic benefits achieved with CARDIZEM are believed to be related to its ability to inhibit the influx of calcium ions during membrane depolarization of cardiac and vascular smooth muscle.

Mechanisms of Action. Although precise mechanisms of its antianginal actions are still being delineated, CARDIZEM is believed to act in the following ways:

1. Angina Due to Coronary Artery Spasm: CARDIZEM has been shown to be a potent dilator of coronary arteries both epicardial and subendocardial. Spontaneous and ergonovine-induced coronary artery spasm are inhibited by CARDIZEM.
2. Exertional Angina: CARDIZEM has been shown to produce increases in exercise tolerance, probably due to its ability to reduce myocardial oxygen demand. This is accomplished via reductions in heart rate and systemic blood pressure at submaximal and maximal exercise work loads.

In animal models, diltiazem interferes with the slow inward (depolarizing) current in excitable tissue. It causes excitation-contraction uncoupling in various myocardial tissues without changes in the configuration of the action potential. Diltiazem produces relaxation of coronary vascular smooth muscle and dilation of both large and small coronary arteries at drug levels which cause little or no negative inotropic effect. The resultant increases in coronary blood flow (epicardial and subendocardial) occur in ischemic and nonischemic models and are accompanied by dose-dependent decreases in systemic blood pressure and decreases in peripheral resistance.

Hemodynamic and Electrophysiologic Effects. Like other calcium antagonists, diltiazem decreases sinoatrial and atrioventricular conduction in isolated tissues and has a negative inotropic effect in isolated preparations. In the intact animal, prolongation of the AH interval can be seen at higher doses.

In man, diltiazem prevents spontaneous and ergonovine-provoked coronary artery spasm. It causes a decrease in peripheral vascular resistance and a modest fall in blood pressure and, in exercise tolerance studies in patients with ischemic heart disease, reduces the heart rate-blood pressure product for any given work load. Studies to date, primarily in patients with good ventricular function, have not revealed evidence of a negative inotropic effect; cardiac output, ejection fraction, and left ventricular end diastolic pressure have not been affected. There are as yet few data on the interaction of diltiazem and beta-blockers. Resting heart rate is usually unchanged or slightly reduced by diltiazem.

Intravenous diltiazem in doses of 20 mg prolongs AH conduction time and AV node functional and effective refractory periods approximately 20%. In a study involving single oral doses of 300 mg of CARDIZEM in six normal volunteers, the average maximum PR prolongation was 14% with no instances of greater than first-degree AV block. Diltiazem-associated prolongation of the AH interval is not more pronounced in patients with first-degree heart block. In patients with sick sinus syndrome, diltiazem significantly prolongs sinus cycle length (up to 50% in some cases).

Chronic oral administration of CARDIZEM in doses of up to 240 mg/day has resulted in small increases in PR interval, but has not usually produced abnormal prolongation. There were, however, three instances of second-degree AV block and one instance of third-degree AV block in a group of 959 chronically treated patients.

Pharmacokinetics and Metabolism. Diltiazem is absorbed from the tablet formulation to about 80% of a reference capsule and is subject to an extensive first-pass effect, giving an absolute bioavailability (compared to intravenous dosing) of about 40%. CARDIZEM undergoes extensive hepatic metabolism in which 2% to 4% of the unchanged drug appears in the urine. In vitro binding studies show CARDIZEM is 70% to 80% bound to plasma proteins. Competitive ligand binding studies have also shown CARDIZEM binding is not altered by therapeutic concentrations of digoxin, hydrochlorothiazide, phenylbutazone, propranolol, salicylic acid, or warfarin. Single oral doses of 30 to 120 mg of CARDIZEM result in detectable plasma levels within 30 to 60 minutes and peak plasma levels two to three hours after drug administration. The plasma elimination half-life following single or multiple drug administration is approximately 3.5 hours. Desacetyl diltiazem is also present in the plasma at levels of 10% to 20% of the parent drug and is 25% to 50% as potent a coronary vasodilator as diltiazem. Therapeutic blood levels of CARDIZEM appear to be in the range of 50 to 200 ng/ml. There is a departure from dose-linearity when single doses above 60 mg are given; a 120-mg dose gave blood levels three times that of the 60-mg dose. There is no information about the effect of renal or hepatic impairment on excretion or metabolism of diltiazem.

INDICATIONS AND USAGE

1. **Angina Pectoris Due to Coronary Artery Spasm.** CARDIZEM is indicated in the treatment of angina pectoris due to coronary artery spasm. CARDIZEM has been shown effective in the treatment of spontaneous coronary artery spasm presenting as Prinzmetal's variant angina (resting angina with ST-segment elevation occurring during attacks).
2. **Chronic Stable Angina (Classic Effort-Associated Angina).** CARDIZEM is indicated in the management of chronic stable angina. CARDIZEM has been effective in controlled trials in reducing angina frequency and increasing exercise tolerance.

There are no controlled studies of the effectiveness of the concomitant use of diltiazem and beta-blockers or of the safety of this combination in patients with impaired ventricular function or conduction abnormalities.

CONTRAINDICATIONS

CARDIZEM is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning ventricular pacemaker, (2) patients with second- or third-degree AV block except in the presence of a functioning ventricular pacemaker, and (3) patients with hypotension (less than 90 mm Hg systolic).

WARNINGS

1. **Cardiac Conduction.** CARDIZEM prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result in abnormally slow heart rates (particularly in patients with sick sinus syndrome) or second- or third-degree AV block (six of 1243 patients for 0.48%). Concomitant use of diltiazem with beta-blockers or digitalis may result in additive effects on cardiac conduction. A patient with Prinzmetal's angina developed periods of asystole (2 to 5 seconds) after a single dose of 60 mg of diltiazem.
2. **Congestive Heart Failure.** Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic studies in humans with normal ventricular function have not shown a reduction in cardiac index nor consistent negative effects on contractility (dp/dt). Experience with the use of CARDIZEM alone or in combination with beta-blockers in patients with impaired ventricular function is very limited. Caution should be exercised when using the drug in such patients.
3. **Hypotension.** Decreases in blood pressure associated with CARDIZEM therapy may occasionally result in symptomatic hypotension.
4. **Acute Hepatic Injury.** In rare instances, patients receiving CARDIZEM have exhibited reversible acute hepatic injury as evidenced by moderate to extreme elevations of liver enzymes. (See PRECAUTIONS and ADVERSE REACTIONS.)

PRECAUTIONS

General. CARDIZEM (diltiazem hydrochloride) is extensively metabolized by the liver and excreted by the kidneys and in bile. As with any new drug given over prolonged periods, laboratory parameters should be monitored at regular intervals. The drug should be used with caution in patients with impaired renal or hepatic function. In subacute and chronic dog and rat studies designed to produce toxicity, high doses of diltiazem were associated with hepatic damage. In special subacute hepatic studies, oral doses of 125 mg/kg and higher in rats were associated with histological changes in the liver which were reversible when the drug was discontinued. In dogs, doses of 20 mg/kg were also associated with hepatic changes; however, these changes were reversible with continued dosing.

Drug Interaction. Pharmacologic studies indicate that there may be additive effects in prolonging AV conduction when using beta-blockers or digitalis concomitantly with CARDIZEM. (See WARNINGS).

Controlled and uncontrolled domestic studies suggest that concomitant use of CARDIZEM and beta-blockers or digitalis is usually well tolerated. Available data are not sufficient, however, to predict the effects of concomitant treatment, particularly in patients with left ventricular dysfunction or cardiac conduction abnormalities. In healthy volunteers, diltiazem has been shown to increase serum digoxin levels up to 20%.

Carcinogenesis, Mutagenesis, Impairment of Fertility. A 24-month study in rats and a 21-month study in mice showed no evidence of carcinogenicity. There was also no mutagenic response in in vitro bacterial tests. No intrinsic effect on fertility was observed in rats.

Pregnancy. Category C. Reproduction studies have been conducted in mice, rats, and rabbits. Administration of doses ranging from five to ten times greater (on a mg/kg basis) than the daily recommended therapeutic dose has resulted in embryo and fetal lethality. These doses, in some studies, have been reported to cause skeletal abnormalities. In the perinatal/postnatal studies, there was some reduction in early individual pup weights and survival rates. There was an increased incidence of stillbirths at doses of 20 times the human dose or greater.

There are no well-controlled studies in pregnant women; therefore, use CARDIZEM in pregnant women only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, exercise caution when CARDIZEM is administered to a nursing woman if the drug's benefits are thought to outweigh its potential risks in this situation.

Pediatric Use. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Serious adverse reactions have been rare in studies carried out to date, but it should be recognized that patients with impaired ventricular function and cardiac conduction abnormalities have usually been excluded.

In domestic placebo-controlled trials, the incidence of adverse reactions reported during CARDIZEM therapy was not greater than that reported during placebo therapy.

The following represent occurrences observed in clinical studies which can be at least reasonably associated with the pharmacology of calcium influx inhibition. In many cases, the relationship to CARDIZEM has not been established. The most common occurrences, as well as their frequency of presentation, are: edema (2.4%), headache (2.1%), nausea (1.9%), dizziness (1.5%), rash (1.3%), asthenia (1.2%), AV block (1.1%). In addition, the following events were reported infrequently (less than 1%) with the order of presentation corresponding to the relative frequency of occurrence.

Cardiovascular:	Flushing, arrhythmia, hypotension, bradycardia, palpitations, congestive heart failure, syncope.
Nervous System:	Paresthesia, nervousness, somnolence, tremor, insomnia, hallucinations, and amnesia.
Gastrointestinal:	Constipation, dyspepsia, diarrhea, vomiting, mild elevations of alkaline phosphatase, SGOT, SGPT, and LDH.
Dermatologic:	Pruritus, petechiae, urticaria, photosensitivity.
Other:	Polyuria, nocturia.

The following additional experiences have been noted:

A patient with Prinzmetal's angina experiencing episodes of vasospastic angina developed periods of transient asymptomatic asystole approximately five hours after receiving a single 60-mg dose of CARDIZEM.

The following postmarketing events have been reported infrequently in patients receiving CARDIZEM: erythema multiforme; leukopenia; and extreme elevations of alkaline phosphatase, SGOT, SGPT, LDH, and CPK. However, a definitive cause and effect between these events and CARDIZEM therapy is yet to be established.

OVERDOSAGE OR EXAGGERATED RESPONSE

Overdosage experience with oral diltiazem has been limited. Single oral doses of 300 mg of CARDIZEM have been well tolerated by healthy volunteers. In the event of overdosage or exaggerated response, appropriate supportive measures should be employed in addition to gastric lavage. The following measures may be considered:

Bradycardia	Administer atropine (0.60 to 1.0 mg). If there is no response to vagal blockade, administer isoproterenol cautiously.
High-Degree AV Block	Treat as for bradycardia above. Fixed high-degree AV block should be treated with cardiac pacing.
Cardiac Failure	Administer inotropic agents (isoproterenol, dopamine, or dobutamine) and diuretics.
Hypotension	Vasopressors (eg, dopamine or levarterenol bitartrate).

Actual treatment and dosage should depend on the severity of the clinical situation and the judgment and experience of the treating physician.

The oral/LD_{50}'s in mice and rats range from 415 to 740 mg/kg and from 560 to 810 mg/kg, respectively. The intravenous LD_{50}'s in these species were 60 and 38 mg/kg, respectively. The oral LD_{50} in dogs is considered to be in excess of 50 mg/kg, while lethality was seen in monkeys at 360 mg/kg. The toxic dose in man is not known, but blood levels in excess of 800 ng/ml have not been associated with toxicity.

DOSAGE AND ADMINISTRATION

Exertional Angina Pectoris Due to Atherosclerotic Coronary Artery Disease or Angina Pectoris at Rest Due to Coronary Artery Spasm. Dosage must be adjusted to each patient's needs. Starting with 30 mg four times daily, before meals and at bedtime, dosage should be increased gradually (given in divided doses three or four times daily) at one- to two-day intervals until optimum response is obtained. Although individual patients may respond to any dosage level, the average optimum dosage range appears to be 180 to 240 mg/day. There are no available data concerning dosage requirements in patients with impaired renal or hepatic function. If the drug must be used in such patients, titration should be carried out with particular caution.

Concomitant Use With Other Antianginal Agents:

1. **Sublingual NTG** may be taken as required to abort acute anginal attacks during CARDIZEM therapy.
2. **Prophylactic Nitrate Therapy**—CARDIZEM may be safely coadministered with short- and long-acting nitrates, but there have been no controlled studies to evaluate the antianginal effectiveness of this combination.
3. **Beta-blockers.** (See WARNINGS and PRECAUTIONS.)

HOW SUPPLIED

Cardizem 30-mg tablets are supplied in bottles of 100 (NDC 0088-1771-47) and in Unit Dose Identification Paks of 100 (NDC 0088-1771-49). Each green tablet is engraved with MARION on one side and 1771 engraved on the other. CARDIZEM 60-mg scored tablets are supplied in bottles of 100 (NDC 0088-1772-47) and in Unit Dose Identification Paks of 100 (NDC 0088-1772-49). Each yellow tablet is engraved with MARION on one side and 1772 on the other.

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Annual Scientific Session

July 25-26, 1985 • Sun Valley, Idaho

THURSDAY, JULY 25

8:00 a.m. **Update on Pathophysiology of Peptic Ulcer Disease**
Keith G. Tolman, MD, *Associate Professor of Medicine*
The University of Utah School of Medicine
Salt Lake City

9:00 a.m. **Dysphagia: A Common Clinical Problem**
Jorge E. Valenzuela, MD, *Professor of Medicine*
University of Southern California School of Medicine
Los Angeles

10:30 a.m. **Evaluation and Surgical Management**
Thomas R. DeMeester, MD, *Professor and Chairman, Department of Surgery*
Creighton University School of Medicine
Omaha

11:30 a.m. **Disorders of Gastric Emptying**
Jorge E. Valenzuela, MD

2:00 p.m. **Implications of Hepatitis B in Health Care Workers**
Keith G. Tolman, MD

3:00 p.m. **Preoperative Evaluation of Patients with Gastroesophageal Reflux**
Thomas R. DeMeester, MD

4:00 p.m. **Panel Discussion**

FRIDAY, JULY 26

8:00 a.m. **Implications of DRG's in Care of the Cancer Patient**
Albert M. Brady, MD
Medical Oncologist in Private Practice
Portland

9:00 a.m. **Thyroid Nodules: A Practical Approach to Management**
Kenneth E. W. Melvin, MD, *Chief of Medicine and Brill Professor*
St Vincent's Hospital
Portland

10:30 a.m. **Pain Control: With Emphasis on Terminal Disease**
Albert M. Brady, MD

11:30 a.m. **Estrogens and Osteoporosis**
Kenneth E. W. Melvin, MD

12:30 p.m. **Adjourn**

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(Continued on Page 592)

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(Continued from Page 590)

PHYSICIANS WANTED

NEUROLOGIST—Wanted Board eligible/certified Neurologist to join a growing neurology practice in a well-established, pre-paid health plan located in Southern California. A busy and varied referral practice is assured. Experience with EMG and EEG is required. Re-location assistance and other benefits offered. Call now for further details. Donald B. Dawson, Director of Physician Staffing, toll-free at (800) 446-2255, in California call (800) 336-2255. FHP Professional Staffing, 400 Oceangate Blvd., Suite 1317, Long Beach, CA 90802. For opportunities in Utah, call Maryalys Poulson collect at (801) 355-1234.

FAMILY PRACTICE, NORTHERN IDAHO. Progressive, established group, with General Surgeon, seeks another physician. Guaranteed salary, modern facility. 35-bed hospital. 60 miles from major city. Scenic area with abundant outdoor activities. Contact D. G. Henriksen, MD, 229 South 8th St., Maries, ID 83861; (208) 245-2591.

WYOMING—ER STAFF POSITION—Emergency Room in Rawlins, WY with moderate volume. Independent contractor status. Malpractice paid. Very flexible schedule. Excellent hunting, fishing, backpacking and skiing in surrounding area. Send Résumé to: Duane Eugene Abels, DO PC, PO Box 1536, Rawlings, WY 82301 or call (307) 324-2221 x115.

PSYCHIATRIST: The University of Wyoming Student Health Service is now interviewing for a psychiatrist to work during Fall, Spring and Summer semesters. Position available Fall 1985, 9½ month position. Candidates must have completed an approved residency and be Board certified in Psychiatry. Candidate will be asked to rotate night call (3 hours) and week-ends (8 hours per day) with primary care physicians. Selected candidate must have demonstrated the ability to work with college age students. Candidate must also demonstrate knowlege and ability to develop innovative mental health care clinics and supervise other mental health providers as well as post graduate students. Candidate must obtain a Wyoming license within six months if not already licensed. Selected candidate will join seven health care providers to care for 10,000 students in Laramie, Wyoming. Salary commensurate with qualifications and experience. The University of Wyoming is an Equal Opportunity/Affirmative Action Employer. Send CV to: Dale C. Brentlinger, MD, Director, Student Health Service, University of Wyoming, University Station Box 3068, Laramie, WY 82071.

PHYSICIANS WANTED

PEDIATRICIAN BE/BC—Full Time—to join well-established academically oriented pediatric practice. Send CV to L. M. Holve, MD, Westside Pediatric Medical Group, 2001 Santa Monica Blvd., Suite 690-W, Santa Monica, CA 90404.

OREGON—North Coast Medical Center, PC seeks a Board-certified Family Physician interested in a full-spectrum practice including OB. The group is also recruiting an Internist, and will include three FP's, two Internists and a General Surgeon. New clinic adjacent to hospital. Thriving coastal setting. Guaranteed salary and benefits. Contact Walter E. Shaffer, MD, 727 South Wahanna Rd., Seaside, OR 97138.

ESTABLISHED SAN FRANCISCO BAY AREA SURGEON—With 27 years of strict referral practice desires dynamic Board-eligible or certified General Surgeon with some Thoracic Surgery experience to become an associate. Send résumé to Box 6467, Western Journal of Medicine, 44 Gough St., San Francisco, CA 94103 or call (415) 797-1770.

INTERNIST needed to join California private practice Internal Medicine group. Excellent opportunity in rapidly growing metro population of 250,000. Close to many recreational and major metropolitan areas. New office with in-house laboratory, radiology, cardiology. Send CV to Box 6466, Western Journal of Medicine, 44 Gough St., San Francisco, CA 94103.

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INTERNIST WANTED to associate with Allergist/Rheumatologist with established practice in San Diego, California. Send Vitae to W. B. Pincus, MD, 2602 First Ave., San Diego, CA 92103.

PHYSICIANS WANTED

ACADEMIC NEUROLOGISTS, General Internists, Cardiologist—wanted for full-time faculty positions. Must be Board admissible or certified, interested in teaching medical students and house staff. Good balance between clinical practice and teaching with research opportunities available. Assistant Professor level with excellent guaranteed salary and benefits. Send CV to Victor H. Kaylarian, DO, Department of Medicine, University of Osteopathic Medicine and Health Sciences, 3200 Grand Avenue, Des Moines, IA 50312. All inquiries confidential.

FAMILY PRACTICE PHYSICIAN—for employment in Community Health Center serving rural hispanic population in Northern New Mexico. Practice includes OB, hospital service, and supervision of two PAs. Scenic mountainous area with easy access to campgrounds and ski slopes. Spanish fluency desirable; excellent benefits package. Contact John Glass at (505) 982-5565, or write to Presybterian Medical Services, PO Box 2267, Santa Fe, New Mexico 87504.

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ASSISTANT PROFESSOR level with excellent guaranteed salary and benefits. Send CV to Victor H. Kaylarian, DO, Department of Medicine, University of Osteopathic Medicine and Health Sciences, 3200 Grand Ave., Des Moines, IA 50312. All inquiries confidential.

NEUROLOGIST (BC/BE) to join small group of academic refugees in medically sophisticated Pacific Northwest location. Abundant recreation. Flexible financial arrangements for energetic, competent and sincere physician. Send CV and three references to Box 6463, Western Journal of Medicine, 44 Gough St., San Francisco, CA 94103.

(Continued on Page 594)

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PHYSICIANS WANTED

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FAMILY PRACTITIONERS for pleasant rural community in southeastern Washington. Close to shopping centers, sports, 4-seasonal recreation, 2 major universities. Modern hospital with up-to-date lab, diagnostic x-ray and surgery. Contact or send CV to: Robert Jepsen, Administrator, Whitman Community Hospital, Box 32, Colfax, WA 99111; (509) 397-3435.

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IDAHO: EXCITING FAMILY PRACTICE AND TIME TO ENJOY THE OUTDOORS. Join group of physicians and nurse practitioners serving five rural communities in Southwest Idaho. Includes interesting obstetrics and health education program. Attractive financial package. Contract Robert H. LeBow, MD, MPH, 1515 Third Street North, Nampa, ID 83651 or call (208) 467-4431.

FAMILY PRACTICE OR INTERNAL MEDICINE: Community Health Center in lovely San Francisco seeks full time Board certified Family Practice or Internal Medicine physician. Available immediately. Position includes clinical and administrative duties. Qualifications to include California license, bilingual (Cantonese/English) ability, and clinical and administrative experiences. Work in HMO very desirable. Good fringe package also includes malpractice insurance and educational leave. Salary commensurate with qualifications. Please send CV to: Personnel, North East Medical Services, 1520 Stockton St., San Francisco, CA 94133.

UNIVERSITY OF WYOMING STUDENT HEALTH SERVICE: The Student Health Service has an opening for a full time physician. The physician must be Board certified in Family Practice or Internal Medicine or Pediatrics, and have approved residency training or extensive practice experience. Applicant must be licensed in the State of Wyoming and have at least two years of primary care experience. Physician to join three full time and three part-time physicians to care for 10,000 students on the campus at Laramie, Wyoming. The Student Health Service has its own laboratory, x-ray, pharmacy and limited emergency services. Salary commensurate with qualifications and experience. The University of Wyoming is an Equal Opportunity/Affirmative Action Employer. Send CV to: Dale C. Brentlinger, MD, Director, Student Health Service, University of Wyoming, University Station Box 3068, Laramie, WY 82071.

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ASSISTANT/ASSOCIATE PROFESSOR. Full-time faculty position available in the Department of Family Practice, University of California, Davis; level of appointment commensurate with academic experience and credentials. Should be Board certified by the American Board of Family Practice with interest, training, and/or experience in teaching, research and academic publication activities. The position will remain open until filled . . . applications will not be accepted after 5/31/85. Send CV to Robert C. Davidson, MD, Chair, Department of Family Practice, University of California, Davis, 2221 Stockton Blvd., Sacramento, CA 95817. The University of California is an affirmative action, equal opportunity employer.

FAMILY PRACTITIONER—Full-time position available for residency trained, Board eligible/Board certified Family Practitioners interested in practicing in a comprehensive care environment. Out-patient care and in-hospital responsibilities are offered in a growing family practice organization. Administrative opportunities also available. For information, call Donald B. Dawson, Director of Physician Staffing, toll-free at (800) 446-2255, in California call (800) 336-2255. FHP Professional Staffing, 400 Oceangate Blvd., Suite 1317, Long Beach, CA 90802. For opportunities in Utah, call Maryalys Poulson collect at (801) 355-1234.

CLINICAS DEL CAMINO REAL, INC. is seeking two Family Practice Physicians to augment its medical practice. Pay range is $4,200 to $4,800 per month, plus share of inpatient work. Fringe benefits include: three weeks vacation, sick leave, tax deferred annuity plan, twelve holidays and an excellent working environment located in Ventura County. Send résumé to: Robert S. Juarez, Executive Director, PO Box 4878, Ventura, CA 93004. Knowledge of Spanish desirable. An EOE.

WASHINGTON: OB/GYN AND PEDIATRICIANS. Expanding established primary care group seeking two of each in independent association. Suburban/rural area 20 miles North of Seattle. New facilities. Dr Ware, Silverlake Medical Center, 1819 100th Pl South East, Everett, WA 98204; (206) 337-0800.

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PHYSICIANS WANTED

RHC FOR DD SEEKS PEDIATRICIAN/CHRONIC CARE. Interdisciplinary team setting. University affiliation encouraged. Submit résumé to R. Doan, MD, Fircrest School, 15230 15th Northeast, Seattle, WA 98155. Apply, Fircrest Personnel, (206) 364-0300 ext 430. EOE.

PHYSICIANS WANTED—Opportunities available in OB/GYN, Ophthalmology, and Orthopaedics in Northern California. Send CV to Box 6469, Western Journal of Medicine, 44 Gough St., San Francisco, CA 94103.

PHYSICIAN WANTED—Unique opportunity in Obstetrics and Gynecology with Multispecialty Private Practice Group in San Francisco bay area. Remuneration based on production, minimal guarantee. Send CV to Box 6471, Western Journal of Medicine, 44 Gough St., San Francisco, CA 94103.

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GENERAL SURGEONS needed for long-term practice opportunity in Western Washington community within two hours of Seattle-Tacoma. Training and experience in Vascular or Pediatric Surgery desirable. Practice support package possible. Send CV and reference to Nancy Friedrich, The Friedrich Group, 9284 Ferncliff N.E., Bainbridge Island, WA 98110.

WASHINGTON COASTAL COMMUNITY serving a population of 65,000 is actively recruiting the following specialists: Otolaryngologist, Anesthesiologist, Urologist, Pediatrician and Orthopedic Surgeons. A variety of practice support options is available, i.e. office space, relocation assistance, etc. Enjoy the support of major West Coast Catholic Hospital System. Community has close proximity to major recreational areas and easy access to Seattle and Portland. For information send CV and references to: Nancy Friedrich, The Friedrich Group, 9284 Ferncliff N.E., Bainbridge Island, WA 98110.

MISCELLANEOUS

PROFESSIONAL LIABILITY POLICY with Mutual Protection Trust (Class 9). Value $28,000. Price $21,000. Terms negotiable. Contact S. E. Garfinkle, MD, or Sebastian Conti, MD, 6403 Coyle Ave. #350, Carmichael, CA 95608; Phone (916) 966-5085. Available June 30, 1985.

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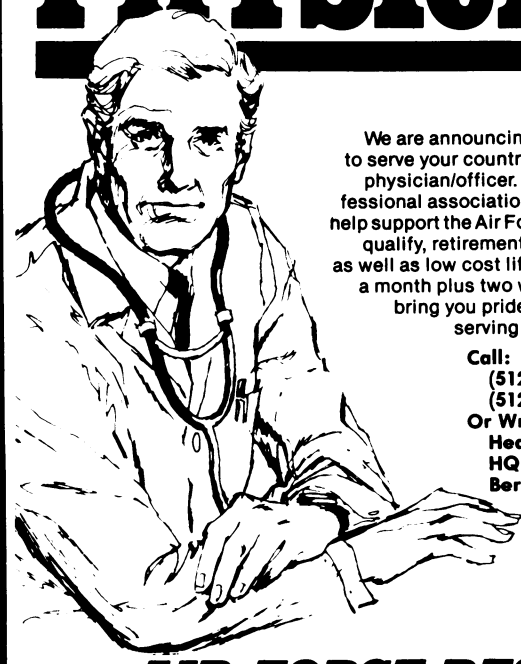
BOARD CERTIFIED FP wants to share office in Huntington Beach, CA. (509) 735-3400, M. S. Cheema, MD, 5219 West Clearwater, Kennewick, WA 99336.

PHYSICIANS



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MEDICAL OFFICE CONDOMINIUM SUITES FOR SALE; Hilltop Professional Building; 1855 San Miguel Dr., Walnut Creek, CA; 800 to 1,200 square foot fully finished suites available; park-like setting; ample parking; for information call App and Edwards Company at (415) 935-6970.

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DEVELOPING HOSPITAL-BASED FAMILY PRACTICE in semi-rural coastal town 25 miles south of San Francisco. Easy access to the entire Bay Area. Contact: Dr Timothy Whelan, St. Catherine Hospital, Moss Beach, CA 94038; (415) 728-3366.

CALIFORNIA: Pediatric, Psychiatric, Opthalmology, OBG, Family, Internal, Surgery, Orthopedic, Podiatry, others. Contact: Mary Bradshaw, Practice Broker/Recruiter, 21 Altamount Dr., Orinda, CA 94563; (415) 376-0762.

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Before prescribing, please consult complete product information, a summary of which follows:

Indications: Relief of moderate to severe depression associated with moderate to severe anxiety.

Contraindications: Known hypersensitivity to benzodiazepines or tricyclic antidepressants. Do not use with monoamine oxidase (MAO) inhibitors or within 14 days following discontinuation of MAO inhibitors since hyperpyretic crises, severe convulsions and deaths have occurred with concomitant use; then initiate cautiously, gradually increasing dosage until optimal response is achieved. Contraindicated during acute recovery phase following myocardial infarction.

Warnings: Use with great care in patients with history of urinary retention or angle-closure glaucoma. Severe constipation may occur in patients taking tricyclic antidepressants and anticholinergic-type drugs. Closely supervise cardiovascular patients. (Arrhythmias, sinus tachycardia and prolongation of conduction time reported with use of tricyclic antidepressants, especially high doses. Myocardial infarction and stroke reported with use of this class of drugs.) Caution patients about possible combined effects with alcohol and other CNS depressants and against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving).

Usage in Pregnancy: **Use of minor tranquilizers during the first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.**

Since physical and psychological dependence to chlordiazepoxide have been reported rarely, use caution in administering Limbitrol to addiction-prone individuals or those who might increase dosage; withdrawal symptoms following discontinuation of either component alone have been reported (nausea, headache and malaise for amitriptyline; symptoms [including convulsions] similar to those of barbiturate withdrawal for chlordiazepoxide).

Precautions: Use with caution in patients with a history of seizures, in hyperthyroid patients or those on thyroid medication, and in patients with impaired renal or hepatic function. Because of the possibility of suicide in depressed patients, do not permit easy access to large quantities in these patients. Periodic liver function tests and blood counts are recommended during prolonged treatment. Amitriptyline component may block action of guanethidine or similar antihypertensives. Concomitant use with other psychotropic drugs has not been evaluated; sedative effects may be additive. Discontinue several days before surgery. Limit concomitant administration of ECT to essential treatment. See Warnings for precautions about pregnancy. Limbitrol should not be taken during the nursing period. Not recommended in children under 12. In the elderly and debilitated, limit to smallest effective dosage to preclude ataxia, oversedation, confusion or anticholinergic effects.

Adverse Reactions: Most frequently reported are those associated with either component alone: drowsiness, dry mouth, constipation, blurred vision, dizziness and bloating. Less frequently occurring reactions include vivid dreams, impotence, tremor, confusion and nasal congestion. Many depressive symptoms including anorexia, fatigue, weakness, restlessness and lethargy have been reported as side effects of both Limbitrol and amitriptyline. Granulocytopenia, jaundice and hepatic dysfunction have been observed rarely.

The following list includes adverse reactions not reported with Limbitrol but requiring consideration because they have been reported with one or both components or closely related drugs:

Cardiovascular: Hypotension, hypertension, tachycardia, palpitations, myocardial infarction, arrhythmias, heart block, stroke.

Psychiatric: Euphoria, apprehension, poor concentration, delusions, hallucinations, hypomania and increased or decreased libido.

Neurologic: Incoordination, ataxia, numbness, tingling and paresthesias of the extremities, extrapyramidal symptoms, syncope, changes in EEG patterns.

Anticholinergic: Disturbance of accommodation, paralytic ileus, urinary retention, dilatation of urinary tract.

Allergic: Skin rash, urticaria, photosensitization, edema of face and tongue, pruritus.

Hematologic: Bone marrow depression including agranulocytosis, eosinophilia, purpura, thrombocytopenia.

Gastrointestinal: Nausea, epigastric distress, vomiting, anorexia, stomatitis, peculiar taste, diarrhea, black tongue.

Endocrine: Testicular swelling and gynecomastia in the male, breast enlargement, galactorrhea and minor menstrual irregularities in the female, elevation and lowering of blood sugar levels, and syndrome of inappropriate ADH (antidiuretic hormone) secretion.

Other: Headache, weight gain or loss, increased perspiration, urinary frequency, mydriasis, jaundice, alopecia, parotid swelling.

Overdosage: Immediately hospitalize patient suspected of having taken an overdose. Treatment is symptomatic and supportive. I.V. administration of 1 to 3 mg physostigmine salicylate has been reported to reverse the symptoms of amitriptyline poisoning. See complete product information for manifestation and treatment.

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